THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

LONDON, S.W. 1.

Balance Sheet and Accounts. December 31st, 1945.

FINANCIAL REPORT.

The Balance Sheet for the year ending December 31st. 1945 shows balances to the credit of the various funds as follows: Capital Fund £679,404; Contingency Reserve £65,329; Sinking (Buildings Depreciation) Fund £66,737; Pension Fund £35,653; Jenner Memorial Research Studentship Fund £9,859 and Bacot Bequest Fund £688.

Changes in investments during the year have been:—

GENERAL FUND:—£12,500 2% Conversion Loan, 1943/5 repaid.

£25,000 3% New Zealand Government Stock, 1945, converted into £25,000 3½% New Zealand Government Stock, 1962/65.

£15,000 2½% National War Bonds and £10,000 3% Savings Bonds, purchased.

SINKING (BUILDINGS DEPRECIATION) FUND:—£9,600, 2% Conversion Stock, 1943/5 repaid. £31,600 3% Savings Bonds, purchased.

PENSION FUND:—£1,000 3% Savings Bonds, purchased.

Income for the year amounted to £94,102 compared with £136,393 in the previous year. Sales of Sera, Vaccines, etc., were £69,654 against £113,398 in 1944.

Expenditure amounted to £73,773 being an increase of £4,513, on last year's figures. Higher cost of Salaries and Wages and Animals mainly account for this increase.

Stocks of Sera on hand at December 31st have the nominal value of £12,323 and Horses of £4,480, but these figures do not appear in the accounts.

Owing to the uncertainty of the future the Governing Body has decided to place the credit balance on the year's working, *viz.*, £20,329 in the Contingency Reserve.

BALANCE SHEET

	£	£
CAPITAL FUND to 31st December 1945:—		
Donations, &c., received to date from the following:—		
Dr. Ludwig Mond (1893)	2,000	
The Berridge Trustees (1893/98)	46,380	
The Grocers' Company (1894)	10,000	
Lord Iveagh (1900)	250,000	
Lord Lister's Bequest (1913/23)	18,904	
William Henry Clarke Bequest (1923/6)	7,114	
Rockefeller Foundation (1935/6)	3,400	
The James Henry Stephens Bequest (per Lloyd's Bank Limited) (1938) ..	500	
Dr. G. A. Davies Bequest (1938)	125	
Other Donations and Legacies (1891-1934)	20,072	
General Fund Income and Expenditure Account:—		
As per Account at 31st December, 1944	320,009	
		679,404
CONTINGENCY RESERVE:—		
As per Account at 31st December 1944	45,000	
Add Balance of Income and Expenditure Account, 1945	20,329	
		65,329
SINKING FUND to 31st December 1945		66,737
PENSION FUND to 31st December 1944	34,679	
Add Balance transferred from Pension Fund Income and Expenditure Account, 1945	974	
		35,653
JENNER MEMORIAL RESEARCH STUDENTSHIP FUND:—		
As per Account at 31st December 1944..	9,549	
Add Balance transferred from Jenner Memorial Research Studentship Fund Income and Expenditure Account, 1945	310	
		9,859
BACOT BEQUEST FUND:—		
As per Account at 31st December 1944	667	
Add Balance transferred from Bacot Bequest Fund Income and Expenditure Account, 1945	21	
		686
CREDITORS		5,95[illegible]

H. H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

£863,62[illegible]

REPORT OF THE AUDITOR[illegible]

We have audited the above Balance Sheet. We have obtained all the information and explanations we h[illegible] which may be partly irrecoverable. Subject to this remark, in our opinion such Balance Sheet is full and [illegible] the best of our information and the explanations given to us and as shown by the books of the Institute.

London, 30th May, 1946.

	£	£
EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA:—		
As per account 31st December 1935, including purchase of freehold site, £6,000		73,548
FREEHOLD LAND, CHELSEA at cost (1912)		169
LEASE OF THE "STUDIOS" CHELSEA, as per last account	546	
Less Amount written off for the year	65	
		481
QUEENSBERRY LODGE ESTATE, ELSTREE—		
Freehold land and buildings as per account 31st December 1912		20,456
FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—		
*At cost less depreciation as per account 31st December 1920	2,472	
Cost of Ultracentrifuges, purchased in 1936, *less* amounts written off ..	340	
		2,812
GENERAL FUND INVESTMENTS (at cost, *less amounts written off*):—		
£80,000 4 per cent. Consolidated Stock, 1957 or after	74,273	
£43,000 3½ per cent. Conversion Stock, 1961, or after	42,916	
£52,000 4 per cent. Funding Stock, 1960-90	45,662	
£64,000 3½ per cent. War Stock	63,408	
£37,000 Local Loans 3 per cent. Stock	20,829	
£101,000 2½ per cent. National War Bonds	101,000	
£123,000 3 per cent. Savings Bonds	123,122	
£3,000 Port of London 3½ per cent. Reg. Stock, 1965-75	2,687	
£8,000 New South Wales 4 per cent. Inse. Stock, 1942-62	8,040	
£25,000 New Zealand Government 3½ per cent. Inscribed Stock, 1962/65 ..	21,989	
£26,100 South Australian Government 3 per cent. Con Stock, 1916 or after ..	16,800	
£2,900 Commonwealth of Australia 3½ per cent. Reg. Stock, 1950-52 ..	2,724	
£25,000 Victorian Government 3 per cent. Con. Inse. Stock, 1929-49 ..	19,800	
£4,000 Western Australia Government 4 per cent. Inscribed Stock, 1942-62 ..	4,081	
£20,000 Southern Railway Preferred Ordinary Stock	13,500	
£6,200 London & North Eastern Railway 3 per cent. Debenture Stock ..	3,961	
£5,000 Gt. Cent & Mid. Rly. Joint Com. 3½ per cent. Guar. Stock	3,623	
£353 London & North Eastern Rly. 4 per cent. First Guaranteed Stock ..	500	
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock ..	7,960	
£15,625 London, Midland & Scottish Rly. 4 per cent. Preference Stock, 1923 ..	11,300	
£18,750 London & North Eastern Rly. 4 per cent. First Preference Stock ..	13,028	
£800 Ontario and Quebec Rly. 5 per cent. Permanent Debenture Stock ..	984	
£3,400 Gas Light & Coke Company Ordinary Stock	3,638	
		605,827
SINKING FUND INVESTMENTS (at cost):—		
£10,200 4 per cent. Funding Stock, 1960-90	9,079	
£20,500 3½ per cent. Conversion Stock, 1961 or after	18,658	
£38,800 3 per cent. Savings Bonds	38,827	
Balance uninvested	173	
		66,737
PENSION FUND INVESTMENTS (at cost):—		
£22,000 4 per cent. Funding Stock, 1960-90	17,165	
£18,000 3½ per cent. Conversion Stock, 1961 or after	15,173	
£3,200 3 per cent. Savings Bonds	3,205	
Balance uninvested	110	
		35,653
JENNER MEMORIAL RESEARCH STUDENTSHIP FUND INVESTMENTS (at cost):—		
£2,650 Southwark & Vauxhall Water Co. 3 per cent. Deb. Stock "B" ..	2,757	
£1,596 Southern Railway 5 per cent. Preference Stock	2,740	
£1,300 Liverpool Corporation 3 per cent. Stock, 1942, or after	1,097	
£2,800 4 per cent. Funding Stock, 1960-90	2,705	
Balance uninvested	560	
		9,859
BACOT BEQUEST FUND INVESTMENT (at cost):—		
£600 3½ per cent. Conversion Stock, 1961 or after	595	
Balance uninvested	93	
		688
(The book value of the above Investments is, in the aggregate, less than their market values at 31st December 1945.)		
STOCK OF ANIMALS	(No value assigned)	
STOCK OF ANTITOXINS	(No value assigned)	
DEBTORS AND PAYMENTS IN ADVANCE		41,054
CASH:—		
At Bankers: On Deposit	1,000	
Current Accounts	5,266	
In hand	76	
		6,342
		£863,626

*Nothing has been charged for depreciation of Furniture, &c. since 1920 as new purchases made during each year to a greater amount than the estimated depreciation (10%) have been written off

TO THE MEMBERS.

In our opinion the above Balance Sheet is properly drawn up so as to exhibit a true and correct view of the state of the Institute's affairs, according to the best of our information and the explanations given to us and as shown by the books of the Institute. Debtors include large amounts due from Government Departments which have not been agreed and required.

COOPER BROTHERS & CO., *Chartered Accountants.* } *Auditors.*

INCOME AND EXPENDITURE ACCOUNTS

INCOME.

General

	£
Dividends on General Fund Investments	22,187
Dividends on Sinking Fund Investments	1,693
Sales of Sera, Vaccines, &c.	69,654
Rent	568
	£94,102

Pension

	£
Dividends on Investments	1,576
	£1,576

Jenner Memorial Research

	£
Dividends on Investments	310
	£310

Bacot

	£
Dividends on Investment	21
	£21

Cancer Research

	£
Balance of Legacy from John George Mills (1937)...	671
	£671

for the year ending 31st. December, 1945.

EXPENDITURE.

Fund.

	£
Rent, Rates, Taxes and Insurance...	2,231
Salaries and Wages of Staff	33,400
Premiums on Federated Superannuation Policies	1,673
Stationery, Printing and Postage	313
Printing of Collected Papers	69
Office Expenses, Auditors' Fee, and Donations	400
Travelling Expenses	257
Gas, Water, Fuel and Electricity	2,566
Nutrition and Protozoological Expenses	580
Bacteriological Expenses...	116
Biochemical Expenses	453
Bio-physics Expenses and Apparatus	600
Serum, Vaccine and Vaccine Lymph Expenses	6,983
Animals	8,388
Animal House Expenses and Forage	9,880
Alterations, Repairs and Renewals	2,642
General Apparatus, New Installations and Furniture	140
Library Expenses	384
General Stores	176
Amounts written off Lease of the "Studios," Chelsea and Ultracentrifuges	405
Sinking Fund (½% per annum on Cost of Buildings and Dividends on Investments) ...	2,117
Balance, transferred to Contingency Reserve	20,329
	£94,102

Fund.

	£
Pensions	602
Balance, transferred to Balance Sheet	974
	£1,576

Studentship Fund.

	£
Balance, transferred to Balance Sheet	310
	£310

Bequest Fund.

	£
Balance transferred to Balance Sheet	21
	£21

Account.

	£
Balance unexpended	671
	£671

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,
1946.

Chelsea Bridge Road,
London, S.W. 1.

June 19th. 1946.

THE GOVERNING BODY.

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S., *Hon. Treasurer.*
PROFESSOR S. P. BEDSON, M.D., B.S., F.R.S.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.
SIR PAUL FILDES, O.B.E., M.A., M.B., B.Ch., F.R.S.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.
THE EARL OF IVEAGH, C.B., C.M.G.

THE COUNCIL.

	REPRESENTING THE
PROFESSOR S. P. BEDSON, M.D., B.S., F.R.S.	Royal Society.
PROFESSOR F. W. ROGERS BRAMBELL, B.A., D.Sc.	Royal Irish Academy.
THE PRESIDENT OF THE ROYAL COLLEGE OF VETERINARY SURGEONS	Royal College of Veterinary Surgeons.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.	University of Cambridge.
PROFESSOR T. J. MACKIE, C.B.E., M.D., M.R.C.P., F.R.S.E.	University of Edinburgh.
V. ZACHARY COPE, M.S., F.R.C.S.	British Medical Association.
PROFESSOR JOHN A. RYLE, M.D. F.R.C.P.	Members of the Institute.
THE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS ...	Royal College of Surgeons of England.
PROFESSOR R. A. PETERS, M.D., F.R.S.	Members of the Institute.
PROFESSOR H. B. MAITLAND, M.D., M.R.C.S., L.R.C.P. ...	Victoria University of Manchester.
PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.S., F.R.S.	Members of the Institute.
SIR HENRY DALE, O.M., G.B.E., M.D. F.R.C.P., F.R.S. ...	" "
PROFESSOR SIR HOWARD W. FLOREY, M.A., PH.D., M.B., B.S., F.R.S.	University of Oxford.
PROFESSOR G. S. WILSON, M.D., B.S., F.R.C.P.	University of London.
LORD MILDMAY OF FLETE, P.C.	Royal Agricultural Society.
SIR WILLIAM WILSON JAMESON, K.C.B., M.D., F.R.C.P., LL.D.	Members of the Institute.
PROFESSOR A. V. HILL, C.H., F.R.S.	" "
PROFESSOR H. S. RAPER, C.B.E., D.Sc., F.R.S.	" "
A. N. DRURY, C.B.E., M.A., M.D., F.R.S.	" "
SIR EDWARD MELLANBY, K.C.B., M.D., F.R.S.	" "
HARRIETTE CHICK, C.B.E., D.Sc.	" "
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S.	" "
THE EARL OF IVEAGH, C.B., C.M.G.	" "
COLONEL RALPH KEY HARVEY	Worshipful Company of Grocers.
MAJOR L. M. E. DENT, D.S.O.	" "
PROFESSOR J. W. BIGGER, M.D., Sc.D., F.R.C.P.	University of Dublin.
THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS ...	Royal College of Physicians, London.
SIR CHARLES J. MARTIN, C.M.G., M.B., LL.D., F.R.S. ...	Members of the Institute.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.	" "
PROFESSOR M. GREENWOOD, D.Sc., F.R.C.P., F.R.S. ...	" "
DR. C. R. HARINGTON, M.A., PH.D., F.R.S.	" "
SIR PAUL FILDES, O.B.E., M.A., M.B., B.CH., F.R.S. ...	" "
SIR PERCIVAL HARTLEY, C.B.E., D.Sc., F.R.S.	" "
J. HENDERSON SMITH, M.B., B.CH.	" "
PROFESSOR M. J. STEWART, M.B., F.R.C.P., LL.D. ...	" "

THE STAFF.

DIRECTOR:

*Alan N. Drury, C.B.E., M.A., M.D., F.R.S.

BACTERIOLOGY and SEROLOGY.

*H. L. Schütze, M.D., B.S.
Muriel Robertson, M.A., D.Sc. (*Protozoology*).
Emmy Klienneberger-Nobel, Ph.D., D.Sc.

EXPERIMENTAL PATHOLOGY.

*A. N. Drury, C.B.E., M.A., M.D., F.R.S.
W. d'A. Maycock, M.D. (*Jointly with Ministry of Health*).
Shirley J. L. Spooner, B.Sc. (*Research Assistant*).

NUTRITION.

*Harriette Chick, C.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).
Alice M. Copping, M.Sc.
Vanda R. G. Pond, B.Sc. (*Research Assistant*).
E. B. Slack, B.A. (*Research Assistant*).
Hannah Henderson Smith.

Medical Research Council External Scientific Staff:

*S. S. Zilva, D.Sc., Ph.D., F.R.I.C.
J. R. Penney, B.Sc., Ph.D., A.R.I.C.
H. A. Painter, B.Sc., A.R.I.C.

BIOCHEMISTRY AND IMMUNOCHEMISTRY.

*W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., (*Reader in Biochemistry in the University of London*). *Principal Biochemist, Elstree*).
Marjorie G. Macfarlane, B.Sc., Ph.D.
R. L. M. Synge, B.A., Ph.D.
P. Ellinger, Dr. Phil. and Med. (*Grantee*).
Marion R. B. Waddell, B.Sc. (*Research Assistant*).
H. Laurell, M.D. (*Sweden*). (*British Council Student*).
K. A. Smith, B.Sc. (*Research Assistant*).
M. M. A. Kader, B.Sc. (*Egyptian Government Student*).
Alexandra Emanuelov, M.D. (*Medical Research Council Grantee*).

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
E. F. McCarthy, M.B., B. Ch., M.Sc.
C. J. B. Bradish, B.Sc. (*Research Student*).
B. Cinader, B.Sc. (*Research Assistant*).
B. R. Record, Ph.D. (*Medical Research Council External Scientific Staff*).

Blood Filtration Unit: Medical Research Council External Scientific Staff.
Margaret Mackay, M.Sc., Ph.D.
Elsie M. Richardson, B.Sc.
Margaret Jones, B.Sc.

PREPARATION AND STUDY OF THERAPEUTIC SERA and BACTERIAL VACCINES.

E. S. Duthie, M.A., M.B., Ph.D.
A. F. B. Standfast, M.A., Dip.Bact.
J. Keppie, Ph.D., M.R.C.V.S.
M. Stack, B.Sc.
M. Zorriassatein, M.D. (*Persia*) (*British Council Student*).

PREPARATION AND STUDY OF VACCINE LYMPH.

*D. McClean, M.B., B.S., M.R.C.S.
*G. H. Eagles, M.D., D.P.H.
C. H. Lack, M.B., B.S.
H. J. Rogers, B.Sc. Ph.D. (*Beit Memorial Research Fellow*).

ADMINISTRATION.

Secretary	A. L. White.
Elstree Secretary and Estate Manager	F. K. Fox.
Assistant Secretary and Accountant	S. A. White, A.L.A.A. (*Royal Signals*).
Librarian	Patricia J. Downman, A.L.A.

NATIONAL COLLECTION OF TYPE CULTURES.

(*Medical Research Council.*)

R. St. John-Brooks, M.A., M.D., D.P.H. (*Curator*). Mabel Rhodes (*Assistant Curator*).
Rosamund Barnes, B.Sc.

Solicitor:
E. S. P. Haynes,
9, New Square, Lincoln's Inn, W.C. 2.

Auditors:
Cooper Brothers & Co.,
14, George Street, Mansion House, E.C. 4.

**Recognised Teacher of the University of London.*

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 19th. 1946.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report on the work of the Institute for the year 1945/6.

GOVERNING BODY.

The Governing Body takes pleasure in recording the conferment of the honour of Knighthood upon Dr. Paul Fildes and that for his conspicuous service to the cause of science Sir John Anderson has been elected to the Fellowship of the Royal Society.

No change has occurred in the personnel of the Governing Body during the year. The Council, at a meeting held on June 18th last, re-elected Professor H. R. Dean, Dr. P. Fildes and Sir Henry Dale as its three representatives on the Governing Body until December 31st 1946.

COUNCIL.

At the Annual General Meeting last year, the three retiring members, Dr. A. N. Drury, Sir Edward Mellanby and Dr. Harriette Chick, each a representative of the Members of the Institute, were re-elected, and vacancies created by the deaths of Sir Humphry Rolleston, Sir Joseph Arkwright, Sir John Ledingham and Lord Moyne were filled by the respective appointments of Mr. V. Zachary Cope, Professor R. A. Peters, Professor A. V. Hill and the Earl of Iveagh.

The three members of Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Sir John Anderson and the Earl of Iveagh, representatives of the Members of the Institute and Colonel Ralph Key Harvey, one of the representatives of the Worshipful Company of Grocers.

MEMBERS.

Invitations to become Members of the Institute have been accepted by Professor A. C. Chibnall, Dr. R. Cruickshank, Dr. R. A. Kekwick, Dr. C. H. Kellaway, Dr. J. E. McCartney, Professor A. A. Miles, Professor R. A. Peters, Dr. E. W. Todd, Dr. Marjory Stephenson and Dr. D. D. Woods, during the year.

STAFF.

Dr. C. R. Amies, Bacteriologist in charge of serum preparation at Elstree resigned his post on December 31st 1945 and has taken up an appointment as Pathologist to the Giza Memorial Ophthalmic Hospital, Cairo. Dr. A. Felix left the Institute in June when he took up a permanent post with the Emergency Public Health Laboratory Service. Dr. D. W. Henderson and Dr. T. F. Macrae also resigned early in 1946 and have respectively taken up appointments with the Ministry of Supply and Messrs. Glaxo.

Dr. W. d'A. Maycock, Technical Adviser to the Blood Transfusion Service of the Ministry of Health, has been appointed a part-time member of the staff whilst still acting in that capacity. Mr. K. A. Smith has been appointed a research assistant in Biochemistry.

Mr. S. A. White still remains on active service abroad.

Dr. E. S. Duthie, Mr. A. F. B. Standfast and Mr. M. Stack have joined the staff at Elstree to undertake the preparation of sera and bacterial vaccines. Dr. Eagles, resumed his work at the Institute on April 1st and has been temporarily appointed to take charge of the preparation of Vaccine Lymph during the enforced absence of Dr. McClean. Dr. C. H. Lack has been appointed to assist in this work.

The Institute has lost the services of two senior laboratory technicians during the year. Mr. W. Sivell, first assistant in the Vaccine Lymph department retired in January after 50 years in the Institute's employment and Mr. G. Kauffman, head bacteriological laboratory assistant died in March after nearly 40 years with the Institute.

All members of the staff evacuated to Cambridge, with the exception of Dr. H. Chick and Mr. Slack have returned to the Institute. Dr. Chick is still enjoying the hospitality of Sir Charles Martin and Mr. Slack that of the University Department of Biochemistry. To Sir Charles Martin, Professor Chibnall and Professor Harris the Governing Body again desires to express its gratitude for the research facilities so willingly afforded to the staff of the Institute.

Various members of the staff have continued to devote time to different Committees set up by the Medical Research Council. Dr. Drury has continued as Chairman of the Committee on the Drying of Human Milk and as a member of the Industrial Health Research Board and the Committee on Jaundice. He has also continued to maintain close contact with the Blood Supply Depots administered by the Council on behalf of the Ministry of Health. In addition he is a member of the Colonial Medical Research Committee and of the Colonial Medical Committee of the Colonial Office.

Dr. Zilva represents the Institute on the Accessory Food Factors' Committee and is a member of its Vitamin A and Vitamin D sub-committees. Dr. Chick is still Secretary of the main Committee; also of its sub-committee on Opportunities for Nutritional Research in Post-war-Europe, and Miss Hume remains Secretary of the Vitamin A sub-committee.

Dr. Robertson is a member and Dr. Macfarlane, Secretary, of the Council's sub-committee on Anærobic Wound Infections.

Accommodation for the Blood Filtration Unit of the Medical Research Council, is being continued at the Institute and in addition accommodation is being provided for the Council's Bacterial Chemistry Unit under the direction of Sir Paul Fildes.

The Governing Body, before surveying the scientific work carried out during the year, desires again to record its appreciation of the continued co-operation and collaboration of the Institute with the Medical Research Council.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Antibodies. Dr. Schutze and Dr. Morgan have been investigating certain types of serum antibody which have been described under such names as incomplete, immature or univalent. Antibody of this kind attaches itself specifically to its appropriate antigen but cannot proceed to the agglutination or precipitation of that antigen. Such antibodies have generally been described as occurring sporadically or as the result of some treatment such as heating and their presence in all normal and immune sera, human or rabbit, have been demonstrated in all those so far examined. It is intended to investigate what bearing, if any, these incomplete antibodies have on the immunological properties of the sera, and how far their presence in the absence of agglutinating or precipitating antibodies indicates establishment of immunity.

Gas Gangrene. Dr. M. G. Macfarlane, in investigations of the effect of *Cl. welchii* alpha-toxin (lecithinase), has studied the distribution of lecithin in muscle, by separation of various fractions and determination of the lipoid constituents. Approximately 50 per cent. of the total lipin and 80 per cent. of the phospholipin is found in the insoluble stroma, *i.e.*, the sarcolemma, but the myosin fraction also contains phospholipin hydrolysable by *Cl. welchii* toxin. The presence of lecithin in the contractile element is of interest in connection with the early loss of contractility in muscle affected by gas gangrene.

Hyaluronidase. In investigations of bacterial hyaluronidase Dr. Rogers (*Beit Memorial Research Fellow*) has found that enzymic hydrolysis products of purified hyaluronic acid differ according to the source from which the hyaluronidase has been prepared. This work together with that of Dr. Hahn in Sweden suggests that each preparation of hyaluronidase may consist of several enzymes, singly responsible for different stages in the degradation of the hyaluronate molecule and which together can completely hydrolyse the polysaccharide to monosaccharides. It is intended to investigate the relation of these various enzymes to the ability of micro-organisms to attack and invade the animal body and also the chemical and immunological differences between them.

Nuclear Structures in Bacteria. Dr. Klieneberger-Nobel has undertaken an examination of the morphological, and particularly the cytological, characters of the group of Myxococci. These investigations have, so far, brought to light a number of distinct characters in which spore-forming bacteria, spore-forming Actinomycetes and microcyst-forming Myxococci differ. On the other hand they have shown that the three mentioned groups have certain characteristics in common, such as the chromatin distribution in some stages and the formation of "fusion cell" at particular but different stages in their life cycles.

Cardiac Hypertrophy. Dr. Drury, in association with Miss Spooner, has continued his observations on the cardiac hypertrophy produced by an arterio venous anastomosis.

Pyrogens and other reacting substances in material used for Transfusion. Miss Spooner has been attempting to find a test which will detect the presence of such substances. Investigations on the temperature, the liberation of histamine in the lung and on the deaminase content of the plasma in guinea-pigs after intraperitoneal or intravenous injections of transfusion fluids known to be pyrogenic or to produce other reactions in man, have not yielded results. Substances suggested as possible substitutes for plasma for transfusion have been tested for toxicity and antigenicity.

Muscle Ischæmia. Miss Macfarlane, in collaboration with Miss Spooner, has studied the chemical changes in ischæmic muscle. It has been found that adenosine triphosphate is not only dephosphorylated but also deaminated during the period of ischæmia and it is possible that the degree of œdema, which results on the re-entry of blood to the occluded limb, can be correlated with the degree of resynthesis of adenosine triphosphate.

Trichomonas Studies. Dr. M. Robertson in collaboration with Dr. W. R. Kerr (Veterinary Research Department, Ministry of Agriculture, Northern Ireland) has continued the investigation of the passive transfer of immune body from the mother to her newly born calf by the ingestion of the colostrum. The sensitisation of the skin of the calf by this means has been demonstrated.

The infection of animals vaccinated parenterally and the attempted re-infection of animals having had an acute infection is being examined and it has been found that parenterally vaccinated animals with circulating antibody and positive skin reactions are susceptible to the disease; the data as regards re-infection after an acute infection is not, so far, conclusive.

Desensitisation of the skin is also being studied and in addition to the already noted desensitisation by injection of antigen or by absorption of antigen from a trichomonous pyometra it has been found there is desensitisation of the skin of sensitised animals upon calving.

Investigation of the serological varieties of *T. fœtus* and a connected study of the non-specific antibody in normal bovine serum is being undertaken by Dr. Robertson who is also carrying out the growth of *T. fœtus*, in mass, for a biochemical study by Dr. Morgan of the nature of this protozoan antigen.

BIOCHEMICAL STUDIES.

Specific Blood-group Substances. Dr. Morgan and Miss M. R. B. Waddell have extended their investigations on the isolation of the human specific blood group substances and have isolated the specific group O-substance. Chemical examination has revealed that the A and O substances are very similar in chemical properties and, so far, no difference in chemical composition has been demonstrated. The O-substance is antigenic when given intravenously to rabbits and induces the formation of quite potent and useful anti-O sera which have been employed in the examination of A, B and O erythrocytes.

Dr. Morgan has examined in some detail the anti-A rabbit sera induced by means of an artificial antigen built up from A-substance of human origin and a conjugated protein component of the bacterial somatic antigen of *Bact. Shigae*.

In collaboration with Surgeon Captain S. G. Rainsford, R.N., Dr. Morgan has investigated the use of rabbit immune serum as a blood grouping agent under conditions which were to some extent peculiar to the Royal Navy and included observations under conditions of special emergency which followed D-day. They found that the use of mixed rabbit anti-A and anti-B immune sera of high titre and avidity reduced the errors of blood grouping when donors were selected rapidly from a group of untyped persons and the mixed serum proved of value in making more reliable, in an emergency, the selection of blood for immediate transfusion.

Dr. Morgan, Miss Dodd and Miss Boorman, of the South-West London Blood Supply Depot, have discovered an interesting phenomenon— the enhancement of the action of immune hæm-agglutinins by human serum. The titration end-point for immune agglutinins was found to be considerably increased when certain compatible human sera were used in place of saline as a diluent. When naturally occurring iso-agglutinin was titrated in serum, however, the titre was found to be the same as that observed using saline as diluent. The differentiation of natural and immune agglutinin by their behaviour in agglutination tests suggests there is a qualitative difference between naturally occurring and immune agglutinins.

"Gramicidin S." Dr. Synge has continued the study of the structural chemistry of "Gramicidin S." An analysis of the products of partial hydrolysis is in progress and is being controlled by synthetic work. On the basis of this and collaborative studies of Dr. Crowfoot, Oxford, Dr. Martin, Leeds, Dr. Sanger, Cambridge and their colleagues, "Gramicidin S" is tentatively formulated as consisting of the amino-acid sequence -*a*-*l*-valyl-*l*-ornithyl-*l*-leucyl-*d*-phenylalanyl-*l*-prolyl- occurring either once (cyclopentapeptide) or twice (cyclodecapeptide) in a closed peptide chain. A number of crystalline derivatives of "Gramicidin S" have been prepared for use in Dr. Crowfoot's crystallographic studies.

Bacterial Antigens. Dr. Morgan, assisted by Mr. K. A. Smith has recommenced his investigations on the nature of the O somatic antigens of some Gram negative bacteria.

Purification and Concentration of antitoxin. Mr. Stack has investigated the nature of the non-protein nitrogen in preparations of refined and concentrated antitoxin prepared by the pepsin process. As much as 10-20 per cent. of the total nitrogen is in this form and its removal by methods of absorption is being investigated.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Human Fibrinogen and Thrombin. Dr. Record (Medical Research Council) is studying the breakdown of fibrinogen under the influence of serum protease, with particular reference to changes in molecular size. The effect of various factors on the clotting of fibrinogen with thrombin has been examined with a view to the definition of a standard fibrinogen preparation for the assay of thrombin.

Tetanus Toxin and Antitoxin. Mr. Cinader is investigating tetanus toxin and antitoxin and their mutual reaction. A method of concentrating tetanus toxin by alcohol precipitation at low temperatures has been devised as a preliminary stage in the purification of the toxin. It has been demonstrated that one of the spurious indicating points observed in the flocculation reaction between crude tetanus toxin and antitoxin is due to the H-antigen of *Cl. tetani* and its antibody. Dr. Keppie is collaborating in this research on its bacterial aspects.

Freeze Drying. Mr. Bradish and Mr. Cinader have made a detailed study of drying conditions in the centrifuge desiccator. The effect of "gelling" prior to freezing on the quality of the dried product in solutions of fibrinogen and gelatin received some emphasis.

In collaboration with Messrs. J. & E. Hall, Ltd, Mr. Bradish has designed and is supervising the erection of a centrifuge freeze drying apparatus with a capacity of 500 units 10 ml. volume.

Fœtal and Maternal Blood. Dr. McCarthy, working in association with Dr. Popjak of St. Thomas' Hospital has made further osmotic pressure measurements and electrophoresis analyses on normal and lipæmic human and rabbit sera, and with Mr. Moore (Medical Research Council of Ireland Grantee) has made some preliminary electrophoretic observations on early fœtal and maternal sheep sera.

Studies on the osmotic pressure measurements on fœtal hæmoglobin have been continued by Dr. McCarthy.

Human Plasma and Plasma Products. The Unit for the preparation of plasma and plasma products administered by the Medical Research Council on behalf of the Ministry of Health has been in continuous operation during the year.

The tray drier, originally designed for the drying of penicillin has been adapted for drying fibrin foam and other materials under aseptic conditions. Throughout the year a steady output of human fibrinogen, fibrin and thrombin has been maintained. The residual ether-extracted plasma proteins have been issued for transfusion. Clinical reports indicate these materials have been found extremely satisfactory in surgical practice.

Dr. M. Mackay (Medical Research Council) and Dr. Kekwick have experiments in progress designed with a view to extending the ether precipitation method to the separation of immune globulins for therapeutic use.

The filtration of large pools of human plasma from hundreds of donors has been discontinued and unfiltered plasma for transfusion is now distributed for drying from pools consisting only of plasma from ten donors.

Routine biochemical tests have been made by Miss E. Richardson (Medical Research Council) to investigate the effect of storage under various conditions on liquid and dried plasma. These have included studies of inorganic phosphate, total non-protein nitrogen, urea and amino-acid nitrogen.

Miss M. Jones (Medical Research Council) in collaboration with Miss Spooner, is investigating the possibility of delaying the absorption of penicillin by incorporating it in fibrinogen products.

The Army Authorities have presented to the Institute, on long loan, the human plasma drying plant used by them during the war. Part of this plant is being erected for the purpose of drying human plasma for civilian needs.

NUTRITIONAL STUDIES.

Nutritive value of different Food Proteins.

i. **Wheat.** Dr. H. Chick and Mr. E. B. Slack have continued their work on the growth-promoting value for young rats of the proteins in wheat. This work was extended in view of the changes introduced by H.M. Government by which a progressive reduction took place in the percentage of wheat grain included in National flour. A set of biological tests, made with flours (of, respectively 70, 80, 85 and 100% extraction) milled from the same grist, confirmed the results of previous work in showing a progressive increase in the growth-promoting value for young rats of the proteins of these flours. The results of analyses at the end of the trials showed that the proportion of the ingested nitrogen which became finally incorporated in the tissues of the growing animals was increased from 23 to 27 per cent as the degree of extraction of flour was raised from 70 to 100%.

ii. **Wheat bran.** The superiority in nutritive value of the proteins in the whole wheat flour over those in white flour made a study desirable of those contained in the outer coat of the grain, more especially in the aleurone layer, which, in the ordinary milling of wheat, is separated with bran and contains about 16% of the total protein of the grain. Biological tests of diets containing a large proportion of commercial bran, which includes the aleurone layer, are difficult to carry out and to interpret, owing to the large proportion of indigestible matter present. Attempts were therefore made to prepare a nitrogenous concentrate from bran, which could be incorporated in a diet, but these were unsuccessful. Accordingly, the nutritive value of a diet

containing white flour as source of protein was compared with a similar one in which one-fifth of this flour was substituted by bran. The result showed an advantage of about 25% in the utilisation for growth of the nitrogen in the bran-white-flour mixture, although the co-efficient of its digestibility was lowered by the admixture with bran.

iii. **Protein Hydrolysates.** At the request of the Protein Requirements Committee of the Medical Research Council, biological tests were made of the nutritive value of the nitrogen as contained in hydrolysed casein compared with that of the nitrogen present in the untreated material. The results showed a deterioriation in the nutritive value of the nitrogen of the hydrolysates which possessed less than one-third of the value of that of the original casein. The growth-promoting value of the enzymic hydrolysate was greatly improved by the addition of a small amount of cystine, suggesting that the deterioration during hydrolysis might be due, at least partly, to the destruction of sulphur-containing amino-acids.

iv. **Milk Substitutes for use as Infant Foods.** Biological tests with young newly weaned rats were made, at the request of the Medical Director of the European Regional Office of U.N.R.R.A., of the nutritive value of the proteins contained in a series of "Maltavena" Emergency Baby Foods, designed to replace milk, in circumstances in which milk may be unobtainable or in very inadequate supply. The common ingredient of these preparations was an extract of malted barley which provided about one-third of the total nitrogen. The remaining two-thirds were derived from wheat flour and skim milk powder, the total amount of protein in these foods being arranged to be about equal to that in human milk. The results showed that the proteins in the foods containing wheat flour and skim milk powder and one containing wheat flour and dried human serum were much inferior in value to those of the milk in the standard diet, but those in the food containing soya flour had a value only very slightly inferior to that of milk proteins. This result is presumably due to the effect of the supplementary action of the proteins contained in the different foods (malt extract, wheat flour, soya flour) included. In addition, the preparations containing soya flour contributed a valuable amount of fat to the diet and an adequate supply of B vitamins. These milk-substitutes baby foods would, however, need supplementation with Vitamins A and D.

v. **Amino-acid composition of the Potato protein "Tuberin."** Under the guidance of Professor Chibnall and his staff, Mr. Slack has made a quantitative analysis of the amino-acid composition of Tuberin, the protein contained in the raw squeezed juice of potatoes and separated by heat coagulation at the iso-electric point. Preliminary tests on the nitrogenous compounds present in the protein-free filtrate after coagulation of the tuberin in potato juice indicated presence of cystine and methionine and the amounts are now being investigated; if present in significant quantity, this fact would account in part at least, for the supplementary nutritive action found by Chick and Cutting to exist between the protein and non-protein fractions of potato juice.

Biological estimations of Vitamins. Miss Copping, with the assistance of Miss Pond, has carried out biological tests of materials for their riboflavin and vitamin B_6 content on behalf of the Vitamin B Sub-committee of the Accessory Food Factors' Committee as part of comparative studies of biological, microbiological and chemical methods of estimating B vitamins. Tests were also made of barley products for a special infant food being prepared for distribution by U.N.R.R.A.

In connection with the development of satisfactory methods for the biological estimation of B vitamins, further investigation of the method for estimating vitamin B_6 has been made by Miss Copping. Owing to wartime changes in the liver extracts available for certain of the dietary supplements required in this test, the method as originally devised became unsatisfactory. Through the kindness of Dr. Robinson and Dr. Emery of Glaxo Laborarories new liver extracts were obtained and these are being used in further tests. If a satisfactory method is evolved it will greatly assist in solving the problem of the relative biological activity of the analogues of vitamin B_6.

Vitamin A. Miss Hume, assisted by Miss Pond, has undertaken chemical investigations on vitamin A.

NICOTINAMIDE AND RELATED COMPOUNDS.

Nicotinamide supply by the intestinal flora of man. Attempts are now being made by Dr. Ellinger in collaboration with Dr. Schütze and Dr. Emanuelov (Medical Research Council grantee) to investigate which species of bacteria are most concerned with the nicotinamide supply and how variation in diet and administration of drugs affect the composition of the intestinal flora as well as the urinary elimination of nicotinamide methochloride. For this purpose, methods of assay worked out first on rats, are now being applied to human volunteers in collaboration with Dr. S. W. Hardwick of West Park Hospital, Epsom.

Formation of nicotinamide from nicotinic acid. Investigations on tissue slices has shown that the amide was formed from the acid in kidney and brain but not in muscles, heart-muscles, spleen, pancreas, blood, intestinal mucous membrane or liver. When glutamine was added in large amounts in a number of experiments, the liver was able to form nicotinamide methochloride from nicotinic acid.

The influence of diet and drugs on the elimination of nicotinamide methochloride by the rat. The influence of some dietary factors connected with the development or cure of pellagra, of some drugs which might affect the bacterial flora, and of carbon tetrachloride which might affect the methylating mechanism in the liver, has been investigated by Dr. Ellinger, using the rat as experimental animal.

Factors influencing the nicotinamide methochloride test in man. The absorption of nicotinamide when administered to human beings by various routes has also been studied in collaboration with Dr. Hardwick. It has been shown that in normal individuals the absorption is quick and equal from subcutaneous tissue, stomach and rectum. They are, however, individual cases with delayed absorption or destruction in stomach and rectum. The role of methyl donators in the methylating mechanism has been studied by administering methionine in addition to test doses of nicotinamide.

Assay methods of nicotinamide and related compounds. With Mr. Abdel Kader (Egyptian Government Student) separate estimations of nicotinamide, nicotinic acid, trigonelline and nicotinuric acid in the same medium, are being undertaken.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Interfering substances in the Roe and Kuether method for the determination of ascorbic acid. Dr. Zilva in collaboration with Dr. Penney has examined critically Roe and Kuether's method for the estimation of ascorbic acid. They were able to extend the specificity of the method because of an observation that some non-ascorbic acid reducing substances reacted more rapidly than the vitamin under certain conditions. They also found that by utilising this differential behaviour of the reaction and by simultaneously performing an assessment by Lugg's method, with corrections suggested by Snow and Zilva, the specificity could be further increased. In addition such procedure supplied some useful information concerning the chemical nature of the interfering substances. The existence of reducing substances hitherto unknown is indicated.

Metabolism of vitamin C. Utilising the newer chemical methods and particularly the knowledge acquired concerning the chemical nature of the reactions, Dr. Zilva in collaboration with Dr. Penney has resumed his work on the metabolism of vitamin C. The immediate purpose of this inquiry is to discover objective criteria for the condition immediately preceding the appearance of scorbutic lesions.

The influence of vitamin C on the metabolism of amino acids. Dr. Zilva in collaboration with Mr. Painter has been studying the influence of vitamin C on the metabolism of certain amino acids. Much time has been devoted to the improvement of the methods of estimation of these amino acids in order to attain the specificity and accuracy required by an investigation of this nature.

Miscellaneous researches. Work is in progress on the part played by diketogulonic acid in the metabolism of the young apple and the influence of light on the vitamin C content of maturing tomato on the plant and in storage.

Investigations on practical problems for the Fighting Services have been concluded during the year.

National Collection of Type Cultures. The Collection continues to be accommodated at Elstree laboratories. During the year under review there was a substantial increase in the number of cultures distributed to workers at home and abroad, amounting to over 5,700 compared with some 4,500 in the previous year. Over 200 strains were lodged by correspondents for maintenance or investigation.

In conclusion, the Governing Body desires to record its great appreciation of the manner in which the Director and all his co-workers, of the scientific, official and technical staffs, have worked together during the period under review to ensure the smooth resumption of the normal activities of the Institute. The transfer from conditions of war to those of peace has involved, and will still involve, difficulties of supply and of readjustment; but the Governors are confident that the Institute is well embarked on a career of new and expanding service to science and to the community.

H. H. DALE,

Chairman of the Governing Body.

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

LONDON, S.W. 1.

Balance Sheet and Accounts. December 31st 1946.

FINANCIAL REPORT.

The Balance Sheet for the year ending December 31st. 1946 shows balances to the credit of the various funds as follows: Capital Fund £679,404; Contingency Reserve £56,539; Sinking (Buildings Depreciation) Fund £69,433; Pension Fund £35,783; Jenner Memorial Research Studentship Fund £10,169 and Bacot Bequest Fund £651.

Investments of the General Fund have been reduced by the sale of £10,000 2½% National War Bonds 1949/51.

Gross Income for the year amounted to £101,624, compared with £94,102 in 1945. Costing adjustments on sales under Government contracts accruing during the years 1942/5 amounting to £10,070 have been deducted from this sum, leaving the nett income at £91,554.

Expenditure amounted to £100,344 against £73,773 last year, the increases in Salaries & Wages, Gas, Water, Fuel & Electricity, Serum, Vaccine & Vaccine Lymph Expenses, Buildings, Alterations, Repairs & Renewals and General Apparatus & New Installations being mainly responsible.

The year's debit balance of £8,790 shown by the accounts has been transferred to the Contingency Reserve.

Stocks of Sera on hand at December 31st have the nominal value of £14,404 and Horses of £3,724. These figures do not appear in the accounts.

BALANCE SHEET

	£	£
CAPITAL FUND to 31st December 1946:—		
Donations, &c., received to date from the following:—		
Dr. Ludwig Mond (1893)	2,000	
The Berridge Trustees (1893/98)	46,380	
The Grocers' Company (1894)	10,000	
Lord Iveagh (1900)	250,000	
Lord Lister's Bequest (1913/23)	18,904	
William Henry Clarke Bequest (1923/6)	7,114	
Rockefeller Foundation (1935/6)	3,400	
The James Henry Stephens Bequest (per Lloyd's Bank Limited) (1938) ..	500	
Dr. G. A. Davies Bequest (1938)	125	
Other Donations and Legacies (1891-1934)	20,972	
General Fund Income and Expenditure Account:—		
As per Account at 31st December, 1944	320,009	
		679,404
CONTINGENCY RESERVE:—		
As per Account at 31st December 1945	65,329	
Less Deficit on Income and Expenditure Account, 1946	8,790	
		56,539
SINKING FUND to 31st December 1946		69,433
PENSION FUND to 31st December 1945	35,653	
Add Balance transferred from Pension Fund Income and Expenditure Account, 1946	130	
		35,783
JENNER MEMORIAL RESEARCH STUDENTSHIP FUND:—		
As per Account at 31st December 1945..	9,859	
Add Balance transferred from Jenner Memorial Research Studentship Fund Income and Expenditure Account, 1946	310	
		10,169
BACOT BEQUEST FUND:—		
As per Account at 31st December 1945	688	
Less Balance transferred from Bacot Bequest Fund Income and Expenditure Account, 1946	37	
		651
CREDITORS		17,363

H. H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

£869.342

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have ments which have not been agreed and which may be partly irrecoverable. Subject to this remark, in our opinion, the Institute's affairs, according to the best of our information and the explanations given to us and as shown by

London, 2nd June, 1947.

31st DECEMBER, 1946.

	£	£
EXPENDITURE ON INSTITUTE BUILDINGS AT CHELSEA:—		
As per account 31st December 1935, including purchase of freehold site, £6,000		73,548
FREEHOLD LAND, CHELSEA at cost (1912)		169
LEASE OF THE "STUDIOS" CHELSEA, as per last account	481	
Less Amount written off for the year	65	
		416
QUEENSBERRY LODGE ESTATE, ELSTREE—		
Freehold land and buildings as per account 31st December 1912		20,456
FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—		
*At cost less depreciation as per account 31st December 1920		2,472
GENERAL FUND INVESTMENTS (at cost, *less amounts written off*):—		
£80,000 4 per cent. Consolidated Stock, 1957 or after	74,273	
£43,000 3½ per cent. Conversion Stock, 1961, or after	42,918	
£52,000 4 per cent. Funding Stock, 1960-90	45,662	
£64,000 3½ per cent. War Stock	63,408	
£37,000 Local Loans 3 per cent. Stock	20,829	
£91,000 2½ per cent. National War Bonds	90,751	
£123,000 3 per cent. Savings Bonds	123,122	
£3,000 Port of London 3½ per cent. Registered Stock, 1965-75	2,687	
£8,000 New South Wales 4 per cent. Inscribed Stock, 1942-62	8,040	
£25,000 New Zealand Government 3½ per cent. Inscribed Stock, 1962/65	21,989	
£26,100 South Australian Government 3 per cent. Con. Stock, 1916 or after	16,800	
£2,900 Commonwealth of Australia 3½ per cent. Registered Stock, 1950-52	2,724	
£25,000 Victorian Government 3 per cent. Con. Inscribed Stock, 1929-49	19,800	
£4,000 Western Australia Government 4 per cent. Inscribed Stock, 1942-62	4,081	
£20,000 Southern Railway Preferred Ordinary Stock	13,500	
£6,200 London & North Eastern Railway 3 per cent. Debenture Stock	3,961	
£5,000 Gt. Cent & Mid. Rly. Joint Com. 3½ per cent. Guaranteed Stock	3,623	
£353 London & North Eastern Rly. 4 per cent. First Guaranteed Stock	500	
£8,650 London, Midland & Scottish Railway 4 per cent. Preference Stock	7,960	
£15,625 London, Midland & Scottish Rly. 4 per cent. Preference Stock, 1923	11,300	
£18,750 London & North Eastern Rly. 4 per cent. First Preference Stock	13,028	
£800 Ontario and Quebec Rly. 5 per cent. Permanent Debenture Stock	984	
£3,400 Gas Light & Coke Company Ordinary Stock	3,638	
		595,578
SINKING FUND INVESTMENTS (at cost):—		
£10,200 4 per cent. Funding Stock, 1960-90	9,079	
£20,500 3½ per cent. Conversion Stock, 1961 or after	18,658	
£38,800 3 per cent. Savings Bonds	38,827	
Balance uninvested	2,869	
		69,433
PENSION FUND INVESTMENTS (at cost):—		
£22,000 4 per cent. Funding Stock, 1960-90	17,165	
£18,000 3½ per cent. Conversion Stock, 1961 or after	15,173	
£3,200 3 per cent. Savings Bonds	3,205	
Balance uninvested	240	
		35,783
JENNER MEMORIAL RESEARCH STUDENTSHIP FUND INVESTMENTS (at cost):—		
£2,650 Southwark & Vauxhall Water Co. 3 per cent. Deb. Stock "B"	2,757	
£1,596 Southern Railway 5 per cent. Preference Stock	2,740	
£1,300 Liverpool Corporation 3 per cent. Stock, 1942, or after	1,097	
£2,800 4 per cent. Funding Stock, 1960-90	2,705	
Balance uninvested	870	
		10,169
BACOT BEQUEST FUND INVESTMENT (at cost):—		
£600 3½ per cent. Conversion Stock, 1961 or after	596	
Balance uninvested	55	
		651
(The book value of the above Investments is, in the aggregate, less than their market value at 31st December 1946.)		
STOCK OF ANIMALS	(No value assigned)	
STOCK OF ANTITOXINS	(No value assigned)	
DEBTORS		58,210
CASH:—		
At Bankers:	2,384	
In hand	73	
		2,457
		£969,342

*Nothing has been charged for depreciation of Furniture, &c. since 1920 as new purchases made during each year to a greater amount than the estimated depreciation (10%) have been written off

TO THE MEMBERS.

required. Debtors include large amounts due from a foreign Government and from British Government Depart-
such Balance Sheet is full and fair and properly drawn up so as to exhibit a true and correct view of the state of the books of the Institute.

COOPER BROTHERS & CO.,
Chartered Accountants. } *Auditors.*

INCOME AND EXPENDITURE ACCOUNTS

INCOME.

General

	£	£
Dividends on General Fund Investments		22,540
Dividends on Sinking Fund Investments		2,272
Sales of Sera, Vaccines, &c.	73,422	
Less Costing adjustment on 1942-5 contracts	10,070	
		63,352
Rent		1,995
Sale of Library Books		1,395
		91,554
Deficit transferred to Contingency Reserve		8,790
		£100,344

Pension

	£
Dividends on Investments	1,597
	£1,597

Jenner Memorial Research

	£
Dividends on Investments	310
	£310

Bacot

	£
Dividend on Investment...	21
Balance transferred to Balance Sheet	37
	£58

Cancer Research

	£
Balance of Legacy from John George Mills (1937)...	671
	£671

for the year ending 31st. December, 1946.

EXPENDITURE.

Fund.

	£
Rent, Rates, Taxes and Insurance...	2,069
Salaries and Wages	39,596
Premiums on Federated Superannuation Policies	1,677
Stationery, Printing and Postage	383
Printing of Collected Papers	63
Office Expenses, Auditors' Fee, and Donations	795
Travelling Expenses	330
Gas, Water, Fuel and Electricity	3,042
Nutrition and Protozoological Expenses	580
Bacteriological Expenses...	456
Biochemical Expenses	819
Bio-physics Expenses	637
Serum, Vaccine and Vaccine Lymph Expenses	10,694
Animals	5,973
Animal House Expenses and Forage	9,344
Buildings, Alterations, Repairs and Renewals	17,362
General Apparatus and New Installations	2,760
Library Expenses	324
General Stores	339
Amounts written off Lease of the "Studios," Chelsea and Ultracentrifuges	405
Sinking Fund (½% per annum on Cost of Buildings plus Dividends on Investments)	2,696
	£100,344

Fund.

	£
Pensions and Gratuity	1,467
Balance transferred to Balance Sheet	130
	£1,597

Studentship Fund.

	£
Balance transferred to Balance Sheet	310
	£310

Bequest Fund.

	£
Purchase of Furniture	58
	£58

Account.

	£
Balance unexpended	671
	£671

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,

1947.

Chelsea Bridge Road,
London, S.W. 1.

June 20th. 1947.

THE GOVERNING BODY.

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S., *Hon. Treasurer.*
PROFESSOR S. P. BEDSON, M.D., M.Sc., B.S., F.R.C.P., F.R.S.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.
SIR PAUL FILDES, O.B.E., M.A., M.B., B.Ch., F.R.S.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.
THE EARL OF IVEAGH, C.B., C.M.G.

THE COUNCIL.

	REPRESENTING THE
PROFESSOR S. P. BEDSON, M.D., M.Sc., B.S., F.R.C.P., F.R.S.	Royal Society.
PROFESSOR F. W. ROGERS BRAMBELL, B.A., D.Sc.	Royal Irish Academy.
THE PRESIDENT OF THE ROYAL COLLEGE OF VETERINARY SURGEONS	Royal College of Veterinary Surgeons.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.	University of Cambridge.
PROFESSOR T. J. MACKIE, C.B.E., M.D., M.R.C.P., F.R.S.E.	University of Edinburgh.
V. ZACHARY COPE, M.S., F.R.C.S.	British Medical Association.
PROFESSOR JOHN A. RYLE, M.D., F.R.C.P.	Members of the Institute.
THE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS ...	Royal College of Surgeons of England.
PROFESSOR R. A. PETERS, M.D., F.R.S.	Members of the Institute.
PROFESSOR H. B. MAITLAND, M.D., M.R.C.S., L.R.C.P. ...	Victoria University of Manchester.
PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.S., F.R.S.	Members of the Institute.
SIR HENRY DALE, O.M., G.B.E., M.D. F.R.C.P., F.R.S. ...	" "
PROFESSOR SIR HOWARD W. FLOREY, M.A., PH.D., M.B., B.S., F.R.S.	University of Oxford.
PROFESSOR G. S. WILSON, M.D., B.S., F.R.C.P.	University of London.
... ...	Royal Agricultural Society.
SIR WILLIAM WILSON JAMESON, K.C.B., M.D., F.R.C.P., LL.D.	Members of the Institute.
PROFESSOR A. V. HILL, C.H., F.R.S.	" "
PROFESSOR H. S. RAPER, C.B.E., D.Sc., F.R.S.	" "
A. N. DRURY, C.B.E., M.A., M.D., F.R.S.	" "
SIR EDWARD MELLANBY, K.C.B., M.D., F.R.S.	" "
HARRIETTE CHICK, C.B.E., D.Sc.	" "
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S.	" "
THE EARL OF IVEAGH, C.B., C.M.G.	" "
PROFESSOR S. R. K. GLANVILLE, M.A., F.S.A.	Worshipful Company of Grocers.
MAJOR L. M. E. DENT, D.S.O.	" "
PROFESSOR J. W. BIGGER, M.D., Sc.D., F.R.C.P.	University of Dublin.
THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS ...	Royal College of Physicians, London.
SIR CHARLES J. MARTIN, C.M.G., M.B., LL.D., F.R.S. ...	Members of the Institute.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.	" "
PROFESSOR M. GREENWOOD, D.Sc., F.R.C.P., F.R.S. ...	" "
DR. C. R. HARINGTON, M.A., PH.D., F.R.S.	" "
SIR PAUL FILDES, O.B.E., M.A., M.B., B.CH., F.R.S. ...	" "
SIR PERCIVAL HARTLEY, C.B.E., D.Sc., F.R.S.	" "
J. HENDERSON SMITH, M.B., B.CH.	" "
PROFESSOR M. J. STEWART, M.B., F.R.C.P., LL.D. ...	" "

THE STAFF.

DIRECTOR:

*Alan N. Drury, C.B.E., M.A., M.D., F.R.S.

BACTERIOLOGY, SEROLOGY, and EXPERIMENTAL PATHOLOGY.

*A. N. Drury, C.B.E., M.A., M.D., F.R.S.
Muriel Robertson, M.A., D.Sc., F.R.S. (*Protozoology*).
Emmy Klieneberger-Nobel, Ph.D., D.Sc.
W. d'A. Maycock, M.B.E., M.D. (*Jointly with Ministry of Health*).
Shirley J. L. Spooner, B.Sc. (*Research Student*).

NUTRITION.

*Harriette Chick, C.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).
Alice M. Copping, M.Sc.
Vanda R. G. Pond, B.Sc. (*Research Assistant*).
Hannah Henderson Smith.

Medical Research Council External Scientific Staff:

*S. S. Zilva, D.Sc., Ph.D., F.R.I.C. (*Honorary*).
H. A. Painter, B.Sc., A.R.I.C.
H. R. Perkins, B.Sc.

BIOCHEMISTRY AND IMMUNOCHEMISTRY.

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., (*Reader in Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
Marjorie G. Macfarlane, D.Sc., Ph.D.
R. L. M. Synge, B.A., Ph.D.
P. Ellinger, Dr. Phil. and Med., F.R.I.C. (*Grantee*).
K. A. Smith, B.Sc., A.R.I.C. (*Grocers' Company Research Student*).
D. Aminoff, B.Sc., (*Research Student*).
M. M. Abdel Kader, B.Sc. (*Egyptian Government Student*).
Alexandra Emanuelowa, M.D. (*Medical Research Council Grantee*).
J. D. Feinberg, M.S., Dr. V.M. (*U.S.A.*).
K. Zakrzewski, M.B., C P.H. (*Rockefeller Fellow*).
B. R. Varella, Dr.Pharm. (*Spain*).

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
E. F. McCarthy, M.B., B.Ch., M.Sc.
C. J. B. Bradish, B.Sc. (*Research Student*).
B. Cinader, B.Sc. (*Jenner Memorial Research Student*).
B. R. Record, Ph.D. (*Medical Research Council External Scientific Staff*).
P. Owren, M.B. (*Visiting Worker*).

Blood Products Research Unit.

Margaret Mackay, M.Sc., Ph.D.
P. V. James, B.Sc.
(*Medical Research Council External Scientific Staff*).

PREPARATION AND STUDY OF THERAPEUTIC SERA.

E. S. Duthie, M.A., M.B., Ph.D.
M. Stack, B.Sc.
G. F. B. Weitz, M.R.C.V.S.
A. Rafyi, (*British Council Student*).

PREPARATION AND STUDY OF VACCINE LYMPH.

*D. McClean, M.B., B.S., M.R.C.S.
C. H. Lack, M.B., B.S.

PREPARATION AND STUDY OF BACTERIAL VACCINES.

A. F. B. Standfast, M.A., Dip.Bact.

†*Appointed Teacher of the University of London.* *Recognised Teacher of the University of London.*

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Bacterial Chemistry Unit.

*Sir Paul Fildes, O.B.E., M.B., B.Ch., F.R.S.
G. P. Gladstone, M.B., B.S., Dip. Bact.
D. Herbert, M.A., Ph.D.
G. A. Howard, M.Sc., Ph.D.
M. R. Pollock, B.A., M.B., B.Ch.
H. N. Rydon, D.Sc., Ph.D., F.R.I.C.
Anne Marie Staub, Dr.Sc. (*Pasteur Institute*).
Jane Pinsent, B.Sc.
G. H. Smith, B.Sc.

National Collection of Type Cultures.

S. T. Cowan, M.D., (*Curator*).
Mabel Rhodes (*Assistant Curator*).
Rosamund Barnes, B.Sc.

Blood Group Research Unit.

R. R. Race, M.R.C.S., L.R.C.P.
Sylvia Lawler. M.B., B.S. (*Research Student*).
Ruth Sanger, B.Sc. (*Australian Red Cross*).

MINISTRY OF HEALTH.

Blood Group Reference Laboratory.

A. E. Mourant, B.M., B.Ch., M.A., D.Phil.

ADMINISTRATION.

Secretary	A. L. White.
Elstree Secretary and Estate Manager	F. K. Fox.
Assistant Secretary and Accountant	S. A. White, A.L.A.A.

Solicitor:

E. S. P. Haynes,

9, New Square, Lincoln's Inn, W.C. 2.

Auditors:

Cooper Brothers & Co.,

14, George Street, Mansion House, E.C. 4.

**Recognised Teacher of the University of London.*

ANNUAL GENERAL MEETING
OF
The Lister Institute of Preventive Medicine,
June 20th. 1947.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report on the work of the Institute for the year 1946/7.

GOVERNING BODY.

No change in the personnel of the Governing Body has taken place during the year. The Council at its last meeting re-elected Professor H. R. Dean, Sir Paul Fildes and Sir Henry Dale as its representatives on the Governing Body until December 31st 1947.

COUNCIL.

At last year's Annual General Meeting, of the three retiring members, Sir John Anderson and the Earl of Iveagh, representatives of the Members of the Institute, were re-elected and Professor S. R. K. Glanville was appointed by the Worshipful Company of Grocers as one of its representatives in succession to Colonel Ralph Key Harvey.

The three members of the Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Major L. M. E. Dent, a representative of the Worshipful Company of Grocers, Professor J. W. Bigger, who represents the University of Dublin, and the President of the Royal College of Physicians, London.

MEMBERS.

The Governing Body records with regret the deaths during the year of Lord Mildmay of Flete, who had represented the Royal Agricultural Society on the Council since 1928, Sir Joseph Barcroft, Sir Almroth Wright and Dr. H. L. Schütze, formerly a Beit Memorial Research Fellow, who joined the bacteriological staff of the Institute in 1913 and was elected a member in 1936. Invitations to become members of the Institute have been accepted by Dr. D. W. Henderson, Dr. A. B. Rosher and Dr. M. G. Macfarlane.

STAFF.

The Governing Body takes pleasure in recording the election of Dr. Muriel Robertson to the Fellowship of the Royal Society in recognition of her many valuable contributions to bacteriology and protozoology.

Dr. Eagles, Dr. Keppie, Mr. Slack and Miss Waddell have resigned their appointments and have taken up other research posts. Mr. G. F. B. Weitz, has joined the Elstree staff and Miss S. L. J. Spooner, Mr. D. Aminoff, Mr. K. A. Smith and Mr. B. Cinader appointed to Research Studentships.

Mr. S. A. White resumed his duties, after four years' war service, in August.

Mr. H. G. Wellington, Chief Engineer since 1913, and Mr. W. A. Lee, Elstree stableman since 1909, have retired on pension. The Governing Body records with pleasure its appreciation of the many years of faithful service they have given to the Institute.

Dr. Drury is a member of the Medical Research Council and the Agricultural Research Council and is also a member of various committees of these Councils. In addition, he is a member of the Colonial Medical Research Committee, and of the Colonial Medical Advisory Committee of the Colonial Office.

Dr. Chick has continued to act as secretary of the Accessory Food Factors' Committee, and Miss Hume as secretary of the Vitamin A sub-committee. Miss Copping is a member of the Vitamin B sub-committee and also gives half her time to editorial and general work connected with "Nutrition Abstracts and Reviews."

The Medical Research Council's Blood Products Research Unit, and also its Bacterial Chemistry Unit under the direction of Sir Paul Fildes, are still accommodated at the Institute. In addition accommodation has been provided for the Council's Blood Group Research Unit and for the Blood Group Reference Laboratory of the Ministry of Health.

The Governing Body, before surveying the scientific work carried out during the year, desires again to record its appreciation of the continued co-operation and collaboration of the Medical Research Council with the Institute.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus Pertussis. Mr. Standfast is undertaking an examination of the characteristics of *H. pertussis*, in particular the virulence, colony appearance and capsule formation, to see if this organism undergoes dissociation due to inherent or environmental factors, and to determine if any of these factors influence the immunizing potency of vaccines.

Gas Gangrene. Dr. Macfarlane has been investigating, with Dr. Keppie, the quantitative distribution of antitoxin extractable from the tissues of rabbits, guinea pigs and rats immunised with *Cl. welchii* toxoid. It has been found that in all three species the lung has the highest antitoxin content relative to the serum titre, but there are differences between the species with regard both to the content in other tissues and the relative proportion of antitoxin in the β- and γ-globulin fractions of the immune sera.

Hyaluronidase. Dr. Rogers has continued his investigations of the bacterial hyaluronidase. It has been found that the chemical properties of the hydrolysates produced by hydrolysing purified potassium hyaluronate with hyaluronidases, differ according to the source from which the enzyme has been obtained. The simplest explanation appeared to be that hydrolysis was not brought about by a single enzyme but by a number of enzymes acting in series. To prove this hypothesis the potency of various samples of hyaluronidase from different sources was measured by (a) the rate of viscosity reduction and (b) by the rate of liberation of reducing sugars. The results obtained using these two methods were different and it is concluded that in the case of streptococcal and staphylococcal hyaluronidase, more than one enzyme is involved.

During the course of this work a new method has been devised whereby very highly potent bacterial hyaluronidase can be produced using only very small amounts of hyaluronate.

Nuclear Structures in Bacteria. Dr. Klieneberger-Nobel has examined cultures of *Fusiformis necrophorus* and has obtained an L_1-like culture from two of the strains which resembles closely the L_1 organism from *Streptobacillus moniliformis*. Both these strains are similar to the *Streptobacillus moniliformis* cultures and are either associations of two dissimilar organisms living in close symbiosis or are modifications of the strains. If the latter case, it must be assumed that an organism can be derived from the parent cultures which is filterable, forms small reproductive granules and no longer contains bacteria proper.

Pyrogens and other reacting substances in material used for Transfusion. Miss Spooner has been continuing her observations upon reacting substances found in transfusion material, and has been chiefly concentrating on the liberation of histamine and adenosine from the perfused lung when such substances are intravenously introduced. In addition she has given help in the testing for toxicity and antigenicity of possible substitutes of plasma for transfusion.

Dr. M. Mackay and Dr. Maycock are investigating certain batches of ether-extracted human plasma, which have been found to cause leucocytosis and have a pronounced irritative action when injected into the unanæsthetized rabbit.

Plasma Substitutes. Dr. Maycock has been investigating batches of dextran, prepared by Professor Stacey at Birmingham University, and comparing their antigenic and blood-pressure restoring properties with those of Swedish dextran, with the object of obtaining material suitable for clinical trial as a substitute for human plasma in certain types of case. More recently some dextran commercially produced in this country has been examined. All the dextran so far investigated has been closely comparable to the Swedish material in its restorative effect on the blood pressure level in the bled anæsthetized animal and the absence of antigenicity.

Muscle Ischæmia. Dr. M. G. Macfarlane, in collaboration with Miss Spooner, continued a study of the chemical changes in the muscles of guinea pigs and rabbits during and after a period of ischæmia. The results suggest that the maintenance of the cycle for the metabolism of carbohydrate is a crucial factor in maintaining the normal permeability of the muscle fibre and that the changes leading to clinical shock after the release of a tourniquet may arise from failure to re-establish this cycle, as indicated by the failure to resynthesise the adenosine-triphosphate decomposed during ischæmia.

Trichomonas Studies. Work on trichomoniasis in cattle has been continued by Dr. Robertson in collaboration with Dr. W. R. Kerr (Veterinary Research Department, Ministry of Agriculture, Northern Ireland).

Re-infection of a group of animals which had had infections of varying severities was carried out during the past year. The results at present indicate that subclinical infections convey no immunity against re-infection. Acute infections do seem to afford some degree of protection against re-infection, but the immunity is not of long duration and broke down upon a third exposure.

Studies on sensitisation and de-sensitisation have been continued. De-sensitisation of the skin at parturition has been confirmed and is being further studied.

Facilities were put at the disposal of the Institute by the Microbiological Research Department, Porton (Ministry of Supply) for working out the bulk production of *Trichomonas fœtus*. This problem has now been solved and a method has been evolved by means of which bulk quantities of the organism can be satisfactorily produced. This material affords a substance for the biochemical study of the antigen by Dr. Morgan and Dr. Feinberg.

Vaccine Lymph. Dr. Lack has been investigating various methods of eliminating the bacterial flora of vaccine lymph. Various antiseptics and the adsorption of the bacteria with a variety of adsorbents have been tried, but so far no method of rendering the lymph bacteriologically sterile without reducing the amount of the virus has been found. During these investigations it was noted that certain bacteria, particularly staphylococci, enhanced the proliferation of vaccinia virus in experimental animals. This adjuvant effect appeared to be proportional to the hyaluronidase produced by the organism. Furthermore, the spread of bacteria appears to be proportional to the hyaluronidase production when staphylococci and virus are injected together, but not when the staphylococci are injected alone. The adjuvant action of hyaluronidase-producing streptococci and the virus appears to be even more striking, and is being investigated.

Work has also been carried out on the cultivation of vaccinia in the chorio-allantois of developing chicks and on the agglutination of fowl red cells by egg lymph which is inhibited by neutralising antibody.

Penicillin. In a study of the conditions governing the formation of penicillinase by organisms of the subtilis group, Dr. Duthie has shown that maximum production of this enzyme is obtained only when penicillin is added continuously during the growth phase of the bacteria. Enzyme production depends on adaptation during growth followed by lysis. Similar experiments in the case of penicillinase-producing staphylococci showed no comparable degree of adaptation following the addition of penicillin. The possibility of producing an antiserum against staphylococcal penicillinase is being investigated, since it is likely that this may be of therapeutic value.

Mr. Standfast has also undertaken work on the possible mechanism of penicillin action with regard to the inhibition of enzyme activity of bacterial suspensions by penicillin.

BIOCHEMICAL STUDIES.

Specific Blood Group Substances. Dr. Morgan and Mr. Aminoff have shown that the electrophoretically homogeneous A-substance, which Dr. Morgan and Dr. King isolated from commercial hog mucin some years ago and showed to possess O- as well as A-specificity, is in fact a mixture of two mucoids. All attempts to separate the component A- and O-substances failed, but a new approach gave the required evidence. Individual pig's stomachs were examined for A- and O-specific blood group character and it was found that of 32 stomachs examined the mucoid material obtained from 17 possessed A character with only weak or no O-specificity, whereas the remaining stomachs showed O character alone and were without A-specificity. It thus became clear that the A-O specific character of the original material was due to the mixed nature of the commercial gastric mucin used The results reveal that the chemical and physical techniques employed are unable to separate the specific A and O blood group substances from mixtures in which these mucoids occur together. Dr. Morgan and Mr. Aminoff have examined further the human A, B and O substances occurring in pseudo-mucinous ovarian cyst fluids.

Dr. Morgan is studying the relationship between the reactivity of erythrocytes of all human groups to agglutination with anti-O sera and the capacity of individuals to secrete the so-called O-substance. The secretion of O-substance by individuals of genotype A_1B is of considerable interest and forms the subject of new investigations on biochemical genetics which Dr. Morgan is now undertaking.

Dr Morgan and Mr. Stack have prepared and examined culture filtrates from *Cl. welchii* (Types A, B, and C) and have found them to contain enzyme systems which will rapidly destroy the specific serological characters of the purified A, B and O substances. The enzyme which attacks the A and B substances is thermolabile and its inactivation enables a preparation of an O specific enzyme to be obtained. The chemical changes taking place during the enzymic destruction of the specific serological characters of the group substances have been investigated together with the action of the enzymes on erythrocytes and stroma of all genotypes.

Gramicidin and Tyrocidine. In July last Dr. Synge was given leave of absence to work in the Fysikalisk-Kemiska Institutionen, Upsala, Sweden. He has studied the adsorption properties of naturally occurring peptides especially gramicidin and tyrocidine. The former appears to be homogeneous when examined in alcoholic solution by the technique of "front analysis" recently developed by Tiselius. Tyrocidine proved not to be homogeneous. Dr. Synge has also been engaged on the elaboration of techniques for the separation of peptides containing aromatic amino-acids from those not containing them and for the differentiation of higher peptides from lower ones containing the same amino-acids.

Bacterial Antigens. Dr. Morgan and Mr. Smith have isolated a further quantity of the O-somatic antigen of *Bact. Shigae* and are elaborating methods suitable for the step-wise degradation of this polymolecular complex which was earlier shown to be a macro-molecule containing phospholipin, polysaccharide and conjugated protein. Special interest is attached to the conjugated component particularly as to the nature of the unidentified prosthetic group. Electrophoretically homogeneous polysaccharide has been quantitatively examined for the component sugars which were previously identified as N-acetyl hexosamine, d-galactose and l-rhamnose.

In collaboration with Dr. Zakrzewski, Dr. Morgan has continued his work on the "non-agglutinating" antibody and has followed the formation in rabbits of this type of immune-body after the injection of small quantities of *Bact. Shigae* and of its purified O-somatic antigen and specific polysaccharide and conjugated protein components. The sera obtained are being examined to determine if the presence of "non-agglutinating" immune body is associated with the establishment of immunity.

Dr. Morgan and Dr. Feinberg, in collaboration with Dr. Robertson, have elaborated methods for the isolation of the main antigenic component from *Trichonomas fœtus* and have succeeded in obtaining an antigenic complex in amount sufficient to allow preliminary chemical studies to be undertaken and the nature of the immune-body induced in response to its inoculation into rabbits, to be investigated.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Blood Clotting Factors. Dr. Record has continued to study the purification of human fibrinogen with special reference to the proportion specifically clotted by thrombin, and to the content of active and unactivated proteolytic enzymes. The molecular kinetic properties of many preparations have been examined and correlated with the chemical data.

Dr. Paul Owren using as basic materials the standard preparations of the Blood Products Unit, examined the further purification of prothrombin with a view to obtaining it entirely free from Factor V.

Tetanus Toxin and Antitoxin. Mr. Cinader, in collaboration with Dr. Keppie, has continued his studies on the interaction between tetanus toxin and antitoxin. With a view to obtaining antitoxic sera showing only one end point by flocculation, horses have been immunised with purified toxin and with toxin-antitoxin floccules. The characteristics of bleedings taken during the course of immunisation are under examination.

The ratio of the $L+$ values for the mouse and guinea pig was found to be smaller for the γ-globulin than for the β-globulin antitoxin.

Freeze Drying. Mr. Bradish has studied the vacuum sublimation of ice in a tray drier and has shown that the rate of vapourisation per unit area per unit time, although 2 to 4 times greater than that obtained in the centrifugal and transfusion bottle driers, is only 1/400th of the ideal, theoretical maximum. This apparent anomaly is related to the fact that molecular collisions with the condenser surface are not all effective in condensation, *i.e.* the condensation coefficient is less than unity.

The tray and small centrifugal freeze-drying plants have handled a considerable volume of material for Institute and outside workers. An experimental transfusion bottle head has been incorporated with the 500 bottle centrifugal freeze-drier mentioned in the last report and both have been subjected to preliminary trials.

Ultrasonic Generator. Mr. Bradish has constructed an ultrasonic generator in which X-cut quartz discs are excited to vibration at the resonant frequency (500 KC/S-1 MC/S) by the application of high radio-frequency voltages. Preliminary ultrasonic intensity measurements have been made in terms of the radiation pressure on a spherical obstacle suspended in a standing wave system. An investigation of the influence of ultrasonic vibrations on the protein molecule is being undertaken.

Fœtal and Maternal Blood. Dr. McCarthy, in collaboration with Dr. Cuthbertson of the Rowett Institute, Aberdeen, has carried out electrophoretic analyses of sera and serum fractions from fœtuses and newborn lambs of ewes kept at different levels of nutrition. Osmotic pressure studies of hæmoglobin were continued.

Human Plasma and Plasma Products. The Unit for the preparation of plasma products administered by the Medical Research Council on behalf of the Ministry of Health has been in operation during the year and a steady output of human fibrinogen, fibrin and thrombin has been maintained.

In October last the erection of the Army drying plant, which had been lent to the Institute by the Army on long loan, was completed and from that date there has been a regular output of dried plasma for transfusion.

Dr. Mackay and Dr. Kekwick, using the ether precipitation method, have developed a procedure for separating the immune globulins from human plasma. The procedure is quite suitable for large scale production and immune globulin separated by this method is undergoing therapeutic trial in association with the Public Health Laboratory Service of the Medical Research Council. Preliminary results in the prophylaxis of measles indicate that the product contains the immune globulins for this disease.

NUTRITIONAL STUDIES.

Nutritive Value of Wheat Proteins. Dr. H. Chick and Mr. Slack, as the result of previous biological tests, found the growth-promoting value for young weanling rats of the mixed proteins from the whole grain to be about 20% greater than that of those from the endosperm (white flour of 70% extraction of the grain.) In these tests, comparison was made between the effects of a series of diets, adequate in other respects, but containing equal sub-optimal amounts of nitrogen derived solely from the different flours studied. In a later series of experiments, an attempt has been made to lower the proportion of protein in the whole wheat diet until the performance of the rats should be equal to that of those receiving a white flour diet containing 2·0% nitrogen (about 12% protein) on dry weight. When the whole wheat flour diet contained 1·5% nitrogen, the rate of weight increase and the relation between this rate and the amount of nitrogen ingested was found to be equal on both diets, thus indicating about a 25% advantage for the proteins of the whole grain.

Mr. Slack continued his studies on the amino-acid composition of the potato protein tuberin and on the amino compound present in the non-protein nitrogenous substances of the potato.

Miss Copping and Miss Pond have been investigating the problem of obtaining complete synthetic diets for rats, suitable for use in estimating the factors of the vitamin B complex biologically

In connection with researches which Dr. Chick has been carrying out at Cambridge, estimations have been made of riboflavin in various barley products.

Miss Pond has been assisting Miss Hume in studies on the investigation of the effects of fat-soluble vitamins on gastric secretion.

NICOTINAMIDE AND RELATED COMPOUNDS.

The fate of nicotinamide methochloride in the rat. From earlier experiments it was known that 15 per cent. of nicotinamide methochloride ingested orally and 60 per cent. after parenteral injection appeared in the urine of man and rat, the remainder not being accounted for. Dr. Ellinger has noted its elimination in the rat's bile and its total destruction, even the splitting up of the pyridine ring by intestinal bacteria.

The effect of *p*-amino-methyl-benzene-sulphonamide ("Ambamide") *in vitro* on intestinal bacteria. Dr. Ellinger, in collaboration with Mr. Abdel Kader and Dr. Emanuelowa, showed that in pure and mixed cultures, growth, acid formation and the production of nicotinamide by *Bact. coli* were stimulated by this substance in smaller and inhibited in larger concentrations, while nicotinamide consuming bacteria such as *Proteus* and *Streptococci* were inhibited by it even in small concentrations.

Nicotinamide supply by the intestinal flora of man. The investigation of the contribution of intestinal bacteria to the nicotinamide requirements of man was continued by Dr. Ellinger and Dr. Emanuelowa, with the co-operation of Dr. Gladstone. It was possible to observe a parallelism between the relative densities of the Gram-negative rod (*Bact. coli*) population of the gut and the urinary elimination of nicotinamide methochloride, both of which were considerably decreased after succinyl sulphathiazole and increased after ambamide intake.

The effect of tryptophane *in vitro* on intestinal bacteria. The finding that tryptophane feeding of rat and man increases the urinary nicotinamide methochloride output has led to a study of the effects of d-l-tryptophane on pure cultures of intestinal bacteria *in vitro* by Dr. Ellinger and Mr. Abdel Kader.

Nicotinamide deficiency after oral administration of penicillin. The observation of the occurrence of "black tongue" in a patient treated with penicillin by oral administration by Dr. F. M. Shattock of Three Counties Hospital, Arlesey, Beds., gave rise to biochemical examination of this case. It could be demonstrated that oral administration of penicillin to this patient, whose nicotinamide status had been low beforehand, caused an acute nicotinamide deficiency which ceased after the discontinuation of penicillin or after administration of nicotinamide but which could be reproduced by renewed oral penicillin administration.

A comparative study of the utilisation of various nicotinamide derivatives by mammals, insects and bacteria. This was carried out by Dr. Ellinger and Mr. Abdel Kader in collaboration with Dr. G. Fraenkel of the Department of Zoology, Royal College of Science. The investigation showed that mono- and di-alkyl and mono-aryl derivatives of nicotinamide could be utilised by the rat, but not di-aryl and cyclohexyl derivatives; a number of bacteria could utilise mainly nicotinamide and nicotinic acid and the behaviour of the insects was intermediate between that of mammal and bacteria. It was shown that insects and some bacteria were able to methylate nicotinamide.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Bacteriological Studies. Sir Paul Fildes has continued his analysis of the stages of synthesis of tryptophan with a view to devising antibacterial substances operating at particular stages.

Dr. Gladstone, in collaboration with Dr. Rydon and Mlle. A. M. Staub, has continued investigations into the production of immunising antigen in anthrax cultures. Further investigations have also been made into the relationship between the production of cellular antigens of *Salm. typhii* and the constituents of the culture medium. A method for the mass production in synthetic media of typhoid organisms having their full complement of antigens is being worked out.

Dr. Herbert and Miss J. Pinsent have been exploiting *M. lysodeikticus* as a source of enzymes liberated from the cell and in particular, have purified bacterial catalase for the first time.

Dr. Pollock has continued his work on factors governing the development of enzymes. He has also clarified concepts of the function of some of the constituents of bacteriological culture media especially in the case of *H. pertussis*.

Dr. Rydon has been working with Sir Paul Fildes on antibacterial substances in the tryptophan series and is also studying the biosynthesis of anthranilic acid.

Mr. Smith is engaged on the preliminary stages of the use of isotopes in analysing the processes of biological synthesis.

Nutritional Studies. Dr. Zilva and Dr. J. R. Penny, in collaboration, endeavoured to find out whether it was possible to correlate the ascorbic acid content to the tissues of guinea pigs with the onset of scurvy. It was found that the variable low values associated with the pre-scorbutic condition could not be utilised as an objective criterion for this purpose. The investigation reveals several points of theoretical interest.

With Mr. Painter, Dr. Zilva has been investigating the influence of *l*-ascorbic acid *in vivo* on the rupturing of the benzene ring in *l*-tyrosine.

Work on the part played by diketogulonic acid in the metabolism of the young apple and the influence of light on the vitamin C content of the maturing tomato, on the plant and in storage, as well as exploratory work on several other problems, is in progress.

Blood Group Studies. The work of this Unit, under Dr. Race, has been almost entirely confined during the year to the Rh blood groups. The main subject of study has been the allelomorph of D, known as D^u. It appears that there are several allelomorphs with similar but not identical effects which produce D^u blood.

Similarly at least two infrequent allelomorphs at the C-c-C^w locus are emerging.

Blood from 1,000 unrelated persons has been tested with all the available varieties of anti-Rh sera, with the view to establishing with more accuracy than before, the gene frequencies in this country, and to collect material to test Fisher's theory that the rarer gene combinations have arisen as the result of crossing-over.

Rather small series of blood samples from Oslo, Cairo, Barcelona and Latvia have been tested, for ethnological purposes, with the various Rh genotype sera.

National Collection of Type Cultures. The National Collection of Type Cultures, which is still housed at Elstree, lost the services of its original curator when Dr. R. St. John-Brooks retired in October 1946. His successor, Dr. Cowan, took up his duties in January 1947.

During 1946 the collection supplied more than 7,000 cultures to workers at home and abroad and helped to re-establish culture collections in several of the countries formerly occupied by German forces. Additions to the collection numbered 131 strains and included a set of serological types of *Streptococcus fæcalis* from Professor A. Grumbach of Zurich.

MINISTRY OF HEALTH.

Blood Group Reference Laboratory. This unit, under the charge of Dr. Mourant, has been concerned with the supply of standard A, B, O and Rh blood grouping sera. In addition it has been preparing to supply the rarer type of sera required for blood grouping work. It has also been concerned with the investigation of difficult cases, and has co-operated very closely with the work of the Medical Research Council's Blood Group Research Unit.

In conclusion, the members of the Governing Body desire to record their great appreciation of the manner in which the Director and all his co-workers, of the scientific, administrative and technical staffs, have worked together during the period under review. The results of that work, as here presented, give them confidence in the continued value and distinction of the Institute's service to science and to humanity.

H. H. DALE,

Chairman of the Governing Body.

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.

AMINOFF, D., MORGAN, W. T. J. AND WATKINS, W. M. — Specific Serological Characters of the Mucoids of Hog Gastric Mucin. *Nature*, 158, 1946.

CHICK, H., AND SLACK, E. B. ... — Malted Foods for Babies. Trials with Young Rats. *Lancet*, Vol. II., 1946.

ELLINGER, P. ... ... — The Fate of Nicotinamide Methochloride in the Rat. *Biochemical Journal*, Vol. 41, 1947.

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ELLINGER, P., FRAENKEL, A., AND ABDEL KADER, M. M. — The Utilisation of Nicotinamide Derivatives and Related Compounds by Mammals, Insects and Bacteria. *Biochemical Journal*, Vol. 41, 1947.

ELLINGER, P., AND HARDWICK, S. W. — The Nicotinamide Saturation Test. *British Medical Journal*, Vol. I., 1947.

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HUMPHREY, J. H. ... ... — Studies on Diffusing Factors. 1. The Kinetics of the Action of Hyaluronidase from Various Sources upon Hyaluronic Acid, with a Note upon Anomalies Encountered in the Estimation of N-Acetyl-Glucosamine. *Biochemical Journal*, Vol. 40, 1946.

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KLIENEBERGER-NOBEL, E. ... The Life Cycle of Sporing *Actinomyces* as Revealed by a Study of their Structure and Septation. *Journal of General Microbiology*, Vol. 1, 1947.

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MORGAN, W. T. J. ... ... Enzymic Decomposition of A, B and O Specific Blood Group Substances. *Nature*, Vol. 158, 1946.

MORGAN, W. T. J. and SCHUTZE, H. Non-Agglutinating Antibody in Human Antisera to *Sh. Shiga* and *S. Typhi*. *British Journal of Experimental Pathology*, Vol. XXVII, 1946.

PAINTER, H. A. and ZILVA, S. S. ... The Influence of *l*-Ascorbic Acid on the rupture of the Benzene ring in high doses of *l*-Tyrosine consumed by Guinea-pigs. *Biochemical Journal*, Vol. 41, 1947.

PENNY, J. R. and ZILVA, S. S. ... The Fixation and Retention of Ascorbic Acid by the Guinea Pig. *Biochemical Journal*, Vol. 40, 1946.

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ROGERS, H. J. ... ... The Influence of Hydrolysates of Hyaluronate upon Hyaluronidase Production by Micro-Organisms. (*Ibid*).

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ROGERS, H. J. AND KNIGHT, B. C. J. G. — The Recognition of Material Present in Horse Muscle Affecting the Formation of α-Toxin by a Strain of *Clostridium welchii*. (*Ibid.*)

SYNGE, R. L. M. ... ... — Partition Chromatography. *The Analyst*, Vol. 71, 1946.

PUBLICATIONS OF MEDICAL RESEARCH COUNCIL UNITS.

GLADSTONE, G. P. ... ... — Immunity to Anthrax: Protective Antigen Present in Cell-Free Culture Filtrates. *British Journal of Experimental Pathology*. Vol. XXVII, 1946.

HANBY, W. E. AND RYDON, H. N. ... — The Capsular Substance of *Bacillus anthracis*. *Biochemical Journal*, Vol. 40, 1946.

POLLOCK, M. R. ... ... — Adaptation of "Nitratase" in Washed Suspensions of Bacteria. *British Journal of Experimental Pathology*, Vol. XXVII, 1946.

THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

LONDON, S.W. 1.

Balance Sheet and Accounts. December 31st 1947.

FINANCIAL REPORT.

The Accounts and Balance Sheet for the year ended 31st December, 1947 are presented in a form consistent with the requirements of the recent Companies Act. They show balances to the credit of the various funds as follow: Capital Fund £695,575; Contingency Reserve £47,030; Specific Funds £108,471 and Bequest Funds £17,601 which figure includes the funds of the Morna Macleod Scholarship received under the Wills of Mr. W. A. and Mrs. I. S. MacLeod during the year.

General Fund Investments have been increased from £595,578 to £606,343.

Income and Expenditure Accounts show the nett income for the year as £82,651 compared with £91,554 in 1946 a reduction mainly accounted for by reduced sales. Expenditure amounted to £92,160 against £100,344 last year. Increases in Gas, Water, Fuel & Electricity and Serum Vaccine and Vaccine Lymph Expenses and decreases in the amounts expended on Animals, Animal House Expenses, Buildings and Alterations and General Apparatus and New Installations accounting principally for the difference.

The year's debit balance of £9,509 shown by the accounts has been transferred to the Contingency Reserve as in the previous year.

Stocks of Sera on hand at December 31st have the nominal value of £18,458 and Horses of £2,356. These values do not appear in the accounts.

BALANCE SHEET

(1946) £		£	£	£
	CAPITAL FUND :—			
	Donations, &c., received to date from the following :—			
2,000	Dr. Ludwig Mond (1893)		2,000	
46,380	Berridge Trustees (1893/98)		46,380	
10,000	Worshipful Company of Grocers' (1894)		10,000	
250,000	Lord Iveagh (1900)		250,000	
18,904	Lord Lister's Bequest (1913/23)		18,904	
7,114	William Henry Clarke Bequest (1923/6)		7,114	
3,400	Rockefeller Foundation (1935/6)		3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)		500	
21,097	Other Donations and Legacies (1891-1938)		21,097	
	General Fund Income and Expenditure Account :—			
	As at 31st December, 1944	320,009		
	Add Surplus on Investment Redeemed	16,171		
320,009			336,180	
679,404				695,575
	CONTINGENCY RESERVE :—			
	As at 31st December 1946		56,539	
56,539	*Less* Deficit on Income and Expenditure Account, 1947		9,509	
				47,030
	CURRENT LIABILITIES :—			
16,691	Creditors and accrued charges		15,904	
672	Balance of Cancer Research Legacy (1937)		672	
				16,576
753,306				759,181
	SPECIFIC FUNDS :—			
69,433	Sinking Fund for Depreciation of Buildings		72,171	
35,783	Pension Fund		36,300	
105,216				108,471
	BEQUEST FUNDS :—			
10,169	JENNER MEMORIAL STUDENTSHIP FUND		10,179	
	MORNA MACLEOD SCHOLARSHIP FUND :—			
	Isobel S. Macleod Bequest	1,500		
	William A. Macleod Bequest	5,205		
	Interest on Investments	45		
—			6,750	
651	BACOT BEQUEST FUND		672	
10,820				17,601
£869,342				£885,253

H. H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have audited the above Balance Sheet. We have obtained all the information and explanations we have which may be partly irrecoverable. Subject to this remark in our opinion such Balance Sheet is full and fair and the best of our information and the explanations given to us and as shown by the books of the Institute.

London, 13th May, 1948.

31st DECEMBER, 1947.

(1946) £		£	£	£
	FIXED ASSETS:—			
	FREEHOLD PROPERTY at cost:			
73,717	Land and Buildings, Chelsea	73,717		
20,456	Queensberry Lodge Estate, Elstree	20,456		
—	House, Bushey	2,049		
	(NOTE: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
			96,222	
	LEASEHOLD PROPERTY:—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,318		
416			351	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
97,061	(*Note*: *Additions and replacements since 31st December, 1920 have been charged to Revenue*)			99,045
595,578	GENERAL FUND INVESTMENTS at cost *less* amounts written off:— (Market Value £656,633)			606 343
	CURRENT ASSETS:—			
—	Stocks of Sera and Horses—no value assigned		—	
58,210	Debtors and Payments in advance		38,902	
2,457	Cash at Bankers and in hand		14,891	
				53,793
753,306				759,181
	SPECIFIC FUNDS:—			
	Investments at cost (Market Value £123,968)		107,083	
	Cash at Bankers		1,388	
105,216				108,471
	BEQUEST FUNDS:—			
	JENNER MEMORIAL STUDENTSHIP FUND INVESTMENTS:—			
	Investments at cost (Market Value £8,881)	9,299		
	Cash at Bankers	880		
10,169			10,179	
	MORNA MACLEOD SCHOLARSHIP FUND INVESTMENTS:—			
	Investments at cost (Market Value £6,263)	6,703		
	Cash at Bankers	47		
—			6,750	
	BACOT BEQUEST FUND INVESTMENTS:—			
	Investment at cost (Market Value £633)	596		
	Cash at Bankers	76		
651			672	
10,820				17,601
£869,342				£885,253

TO THE MEMBERS.

required. Debtors include an amount of £17,285 due from a foreign Government which has not been agreed and properly drawn up so as to exhibit a true and correct view of the state of the affairs of the Institute according to

COOPER BROTHERS & CO., *Chartered Accountants.* } *Auditors.*

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1946) £		£
39,596	Salaries and Wages	39,834
1,677	Premiums on Federated Superannuation Policies	1,781
2,069	Rent, Rates and Insurance	1,676
3,042	Gas, Water, Fuel and Electricity	3,722
446	Stationery, Printing and Postage	556
659	Office Expenses and Donations	515
136	Auditors' Fee	136
330	Travelling Expenses	360
819	Biochemical Expenses	815
456	Bacteriological and Experimental Pathology Expenses	480
580	Nutrition Expenses	318
637	Bio-physics Expenses	493
10,694	Serum, Vaccine and Vaccine Lymph Expenses	14,247
5,973	Animals	3,549
9,344	Animal House Expenses and Forage	5,880
17,362	Buildings, Alterations, Repairs and Renewals	12,898
2,760	General Apparatus and New Installations	1,336
324	Library Expenses	474
339	General Stores	287
	Amounts written off:	
65	Leasehold Property	65
940	Ultracentrifuges	—
2,696	Sinking Fund for Freehold Buildings plus Interest on Investments	2,738
£100,344		£92,160

PENSION

£		£
1,467	Pensions and Gratuity (1946)	1,089
130	Balance transferred to Balance Sheet	517
£1,597		£1,606

JENNER MEMORIAL

£		£
—	Stipend of Student	300
310	Transferred to Balance Sheet	10
£310		£310

MORNA MACLEOD

		£
—	Transferred to Balance Sheet	45
—		£45

BACOT

£		£
58	Purchase of Furniture	—
—	Transferred to Balance Sheet	21
£58		£21

for the year ended 31st December, 1947.

Fund.

(1946) £		£	£
	Interest and Dividends (gross):		
22,540	General Fund Investments	21,981	
2,272	Sinking Fund Investments	2,314	
			24,295
63,352	Sales of Sera, Vaccines, Vaccine Lymph, &c.		53,514
1,995	Rent		4,842
1,395	Sale of Library Books		—
8,790	Deficit transferred to Contingency Reserve		9,509
£100,344			£92,160

Fund.

£		£
1,597	Interest on Investments (gross)	1,606
£1,597		£1,606

Studentship Fund.

£		£
310	Interest on Investments (gross)	310
£310		£310

Scholarship Fund.

		£
—	Interest on Investments (gross)	45
—		£45

Bequest Fund.

£		£
21	Interest on Investment (gross)	21
37	Transferred to Balance Sheet	—
£58		£21

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body, 1948.

Chelsea Bridge Road,
London, S.W. 1.

June 16th, 1948.

THE GOVERNING BODY.

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S., *Hon. Treasurer.*
PROFESSOR S. P. BEDSON, M.D., M.Sc., B.S., F.R.C.P., F.R.S.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.
SIR PAUL FILDES, O.B.E., M.A., M.B., B.Ch., F.R.S.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.
THE EARL OF IVEAGH, C.B., C.M.G.

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HARRIETTE CHICK, C.B.E., D.Sc.	„ „
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S.	„ „
THE EARL OF IVEAGH, C.B., C.M.G.	„ „
PROFESSOR S. R. K. GLANVILLE, M.A., F.S.A.	Worshipful Company of Grocers.
MAJOR L. M. E. DENT, D.S.O.	„ „
PROFESSOR J. W. BIGGER, M.D., Sc.D., F.R.C.P.	University of Dublin.
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J. HENDERSON SMITH, M.B., B.CH.	„ „
PROFESSOR M. J. STEWART, M.B., F.R.C.P., LL.D. ...	„ „

THE STAFF.

DIRECTOR:

*Alan N. Drury, C.B.E., M.A., M.D., F.R.S.

BACTERIOLOGY, SEROLOGY, and EXPERIMENTAL PATHOLOGY.

*A. N. Drury, C.B.E., M.A., M.D., F.R.S.
Muriel Robertson, M.A., D.Sc., F.R.S. (*Honorary*)
Emmy Klieneberger-Nobel, Ph.D., D.Sc.
W. d'A. Maycock, M.B.E., M.D. (*Jointly with Ministry of Health*).
Shirley J. L. Spooner, M.Sc. (*Research Assistant*).

NUTRITION.

*Harriette Chick, C.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).
Alice M. Copping, M.Sc.
Patricia J. Crowe, B.Sc. (*Research Assistant*).
Hannah Henderson Smith.

Medical Research Council External Scientific Staff:

*S. S. Zilva, D.Sc., Ph.D., F.R.I.C. (*Honorary*).
H. A. Painter, B.Sc., A.R.I.C.
H. R. Perkins, B.Sc.

BIOCHEMISTRY AND IMMUNOCHEMISTRY.

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., (*Reader in Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
Marjorie G. Macfarlane, D.Sc., Ph.D.
R. L. M. Synge, B.A., Ph.D.
P. Ellinger, Dr. Phil. and Med., F.R.I.C. (*Grantee*)
A. T. James, B.Sc., Ph.D.
K. A. Smith, B.Sc., A.R.I.C. (*Grocers' Company Research Student*).
D. Aminoff, B.Sc., (*Research Student*).
M. M. Abdel Kader, B.Sc. (*Egyptian Government Student*).
Alexandra Emanuelowa, M.D. (*Medical Research Council Grantee*).
J. D. Feinberg, M.S., Dr. V.M. (*U.S.A.*).
E. F. Annison, B.Sc. (*Medical Research Council Student*).

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
E. F. McCarthy, M.B., B.Ch., M.Sc.
C. J. B. Bradish, B.Sc. (*Research Student*).
B. Cinader, B.Sc. (*Jenner Memorial Research Student*).
J. W. Lyttleton, M.Sc. (*Beit Memorial Research Fellow*).

Blood Products Research Unit.

Margaret Mackay, M.Sc., Ph.D.
P. V. James, B.Sc.
Betty G. Balfour, M.Sc.
Noreen M. F. Haysom, B.Sc.
(*Medical Research Council External Scientific Staff*).

PREPARATION AND STUDY OF THERAPEUTIC SERA.

E. S. Duthie, M.A., M.B., Ph.D.
M. Stack, B.Sc.
G. F. B. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc.

PREPARATION AND STUDY OF VACCINE LYMPH.

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.B., B.S.

PREPARATION AND STUDY OF BACTERIAL VACCINES.

A. F. B. Standfast, M.A., Dip.Bact.
Margaret P. D. Pile, B.Sc.

†*Appointed Teacher of the University of London.* **Recognised Teacher of the University of London.*

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Bacterial Chemistry Unit.

*Sir Paul Fildes, O.B.E., M.B., B.Ch., F.R.S.
G. P. Gladstone, M.B., B.S., Dip. Bact.
D. Herbert, M.A., Ph.D. (*Leverhulme Research Fellow*).
G. A. Howard, M.Sc., Ph.D.
M. R. Pollock, B.A., M.B., B.Ch. (*Leverhulme Research Fellow*).
Anne Marie Staub, Dr. es Sc. (*Pasteur Institute*).
Barbara Boughton, B.Sc. (*Leverhulme Research Student*).
Ruth M. M. Jordan, B.A. (*Leverhulme Research Student*).
D. Kay, B.Sc. (*Leverhulme Research Student*).
Jane Pinsent, B.Sc. (*Leverhulme Research Student*).
G. H. Smith, B.Sc. (*Leverhulme Research Student*).
S. D. Wainwright, B.A. (*Leverhulme Research Student*).

National Collection of Type Cultures.

S. T. Cowan, M.D., Dip. Bact., (*Curator*).
Constance Shaw, M.Sc., Dip. Bact.
Mabel Rhodes.
Mary G. Jennens, B.Sc.

Blood Group Research Unit.

R. R. Race, Ph.D., M.R.C.S., L.R.C.P.
Sylvia Lawler, M.B., B.S. (*Research Student*).
Ruth Sanger, B.Sc. (*Australian Red Cross*).
Doreen Whitaker, B.Sc.
Rosamund Jefferis, B.Sc.

MINISTRY OF HEALTH.

Blood Group Reference Laboratory.

A. E. Mourant, B.M., B.Ch., M.A., D.Phil.
Elizabeth W. Ikin, B.Sc.

ADMINISTRATION.

Secretary	A. L. White.
Elstree Secretary and Estate Manager	F. K. Fox.
Assistant Secretary and Accountant	S. A. White, A.L.A.A.

Solicitor:

E. S. P. Haynes,

9, New Square, Lincoln's Inn, W.C. 2.

Auditors:

Cooper Brothers & Co.,

14, George Street, Mansion House, E.C. 4.

*Recognised Teacher of the University of London.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 16th. 1948.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report on the work of the Institute for the year 1947/8.

GOVERNING BODY.

No change in the personnel of the Governing Body has taken place during the year. The Council at its last meeting re-elected Professor H. R. Dean, Sir Paul Fildes and Sir Henry Dale as its representatives on the Governing Body until December 31st, 1948.

COUNCIL.

At last year's Annual General Meeting, the three retiring members of Council, Major L. M. E. Dent, Professor J. W. Bigger and the President of the Royal College of Physicians, London, were re-elected and Sir William C. Dampier appointed by the Royal Agricultural Society in succession to the late Lord Mildmay of Flete.

The three members due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Sir Charles Martin, Lord Horder and Professor M. Greenwood, each a representative of the Members of the Institute.

MEMBERS.

The Governing Body records with regret the death during the year of Professor J. McIntosh, who had been a member since 1931.

No new members have been elected during the period under review.

STAFF.

Dr. Muriel Robertson retired from the service of the Institute on attaining the age limit in April last. At a meeting held on March 24th last the following resolution was minuted :

> "That the Governing Body on the occasion of Dr. Muriel Robertson's retirement from her appointment with the Institute desires to offer her its warmest wishes for a long period of health, happiness and continued activity and also to record its appreciation of the high value of her work during her 39 years' connection with the Institute, first as Assistant to the late Professor E. A. Minchin, University of London Professor of Protozoology and since 1910, as a member of the Institute's scientific staff, during which period she has made many notable contributions to scientific knowledge, the value of which has been recognised by her election to the Fellowship of the Royal Society."

The Governing Body note with pleasure that Dr. Robertson is continuing her work in the Institute in an honorary capacity under a grant from the Agricultural Research Council.

Dr. C. H. Lack resigned in January on taking up an appointment as Pathologist at the Royal National Orthopædic Hospital and Dr. L. H. Collier has been appointed as his successor. Miss V. R. G. Pond resigned in May and Miss P. J. Crowe has joined the staff of the Nutrition

Unit in her stead. Miss S. J. L. Spooner, former Research Student, Miss L. Lorenz and Miss M. P. D. Pile have taken up temporary staff appointments.

Mr. C. E. Groom retired on pension in December after 28 years' service at Elstree.

The Bacterial Chemistry Unit, under the direction of Sir Paul Fildes, the Blood Products Research Unit and the Blood Group Research Unit of the Medical Research Council are still accommodated at the Institute, as is also the Blood Group Reference Laboratory of the Ministry of Health.

The Governing Body, before surveying the scientific work carried out during the year, once again desires to record its appreciation of the continued co-operation and collaboration of the Medical Research Council with the Institute.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus Pertussis. Mr. A. F. B. Standfast has continued his work on the characteristics of *H. pertussis,* investigating the virulence for mice of freshly isolated strains.

Dr. J. O. Irwin, London School of Hygiene and Tropical Medicine, has carried out a statistical examination of the results obtained so far on 40 strains, which shows that the difference in virulence for mice is statistically significant and the arbitrary divisions of high, medium and low virulence can be made.

A further series of freshly isolated strains is being tested to try and determine if the factors involved in virulence also influence the immunizing properties of whooping cough vaccines. At the same time, an investigation of Kendrick's mouse test for potency of whooping cough vaccines is being carried out.

Bacterial Cytology. Dr. Klieneberger-Nobel, working on study leave at the Hygiene-Institut, Zurich, devised methods which allow the demonstration of capsules, slime envelopes of bacteria and mucoid substances surrounding and embedding capsulated organisms. It has been shown that capsules are distinct from the other mucoid materials. On her return, she extended these investigations and with the co-operation of Dr. F. Kauffman (Copenhagen) has examined a number of his serological typed strains from the Coli- and Salmonella- groups. She has shown that all the Coli strains possessing an A-antigen produce a delicate capsule or capsular edging.

Pyrogens and other reacting substances in material used for transfusion. Dr. M. Mackay and Dr. W. d'A. Maycock completed their investigation of certain batches of ether-extracted plasma which had caused reactions in human beings, and found that they contained dangerously high concentrations of sodium citrate.

Miss S. J. L. Spooner, using the liberation of histamine in the perfused guinea pig's lung as an indication of tissue damage, has tested certain materials used for transfusion and known to give reaction in man, such as human plasma and serum, and casein hydrolysates. None of the transfusion materials tested liberated histamine from the guinea-pig lung.

Plasma Substitutes. Dr. Maycock has continued his investigations of dextran. All the experimental batches received have been found to be non-toxic and non-antigenic and no clinical or histological changes have been observed in animals after large doses. The disappearance of dextran from the blood stream appears to follow approximately the same course as that reported by the Swedish workers. No effects on the opsonic activity of leucocytes or resistance to infection nor evidence of renal damage have been observed. A precipitating serum has been prepared which will detect dextran in low concentrations in human and rabbit serum and urine, and in various tissue extracts. Arrangements have been made with the Medical Research Council's Blood Transfusion Research Unit and Burns Unit for clinical trial of the material. Miss Spooner has co-operated in some of this work.

Trichomonas Studies. Work on trichomoniasis in cattle has been continued by Dr. M. Robertson in collaboration with Dr. W. R. Kerr (Veterinary Research Department, Ministry of Agriculture, Northern Ireland).

The study of re-infection in cattle revealed the presence of specific Trichomonas antibody in the uterine secretion of animals which had been infected with *Trichomonas fœtus* and also in animals which had had Trichomonas antigen instilled into the uterus. This localisation of antibody is being further studied and attempts are being made to elucidate its source.

The work on desensitisation has been continued and the blood picture in regard to the leucocyte counts in being correlated with specific desensitisation by absorption of antigen and with non-specific desensitisation at parturition.

Collaboration with Dr. W. T. J. Morgan and Dr. J. D. Feinberg on this subject is being continued. A haptene has been produced which has proved to be a useful substance for intradermal injection and is being used for the skin tests of experimental animals.

Vaccine Lymph. Dr. C. H. Lack has completed his investigation of the synergism of certain gram positive cocci and vaccinia virus. He found that hyaluronidase is one of the principal factors in the enhancement of mixed virus and coccal infections. His observations explain the increased yield of vaccine pulp and virus due to the presence of cocci in routine production of vaccine lymph and may shed some light on the fulminating streptococcal and staphylococcal infections associated with smallpox. During the course of this investigation fibrinolysis by thirty strains of staphylococci was studied and it was found that, like steptococci, some staphylococci bring about lysis of human and rabbit fibrin clots by activating plasma trypsin.

Specific Anti-Sera. Mr. G. F. B. Weitz has been carrying out experiments relating to the study of precipitating antisera against the blood of man and animals with the object of identifying blood meals of blood-sucking insects.

Preliminary work has been chiefly concerned with the methods of dosage in rabbits with the view of obtaining a high degree of specificity. Even under optimum conditions such sera provided only relatively low specificity. Studies are being followed on the use of various species of animals as producers of precipitating serum and the value of these in obtaining a higher degree of specificity.

The absorption of non-specific fractions is also being studied.

Enzymes. Dr. E. S. Duthie and Miss L. L. Lorenz have studied the inhibitory action of normal and immune sera on pancreatic trypsin and on bacterial proteases, and have shown that while the normal serum inhibitor is associated with the albumin fraction, the inhibitor against bacterial proteases in either normal or immune sera is associated with the globulin fraction. The majority of bacteria produce a non-substrate specific protease which is inhibited by serum and certain pathogenic bacteria produce, in addition, a specific gelatinase which is not inhibited. The latter is closely associated with the collagen splitting enzyme, but is not identical with it.

BIOCHEMICAL STUDIES.

The chemical basis of blood group specificity. Dr. Morgan and Mr. D. Aminoff have continued their studies on the nature of the human specific blood group substances and have isolated the group A-substance. Judged by its behaviour in the ultracentrifuge and electrophoresis apparatus, by its serological and chemical properties and by the products of acid and alkaline hydrolysis, the material is homogeneous and is therefore suitable for detailed chemical examination. A start has already been made on the isolation and identification of the component sugars, amino sugars and amino-acids.

Dr. Morgan has attempted to clarify the position of the so-called O-substances and determine the relationship of this substance to the group agglutinogens A and B. As a result of his investigations it would appear that the material designated as O-substance throughout the literature is not a product of the *O* gene but is a primary or basic substance, heterogenetic in character, which is present in the majority of erythrocytes. It is proposed to call this material

"H-substance" and, with the assistance of Mr. E. F. Annison, methods are being developed for its isolation from pseudomucinous ovarian cyst fluids. During the course of this work Dr. Morgan detected in red-cell extracts a substance with the serological properties of a true O-substance, a product of the *O* gene. This substance, hitherto undiscovered, has been considered by many workers to be absent from the erythrocyte surface owing to the recessive character of the *O* gene. The isolation and characterisation of the O-substance is being vigorously pursued.

Mr. M. Stack and Dr. Morgan have continued their attempts to separate the enzymes in filtrates of *Cl. welchii* which inactivate the serological characters of the blood group substances. Although the separation has not yet been accomplished satisfactorily, very potent enzyme preparations have been prepared and used to destroy the serological properties of stroma, erythrocyte extracts and purified group substances. The decomposition of certain mucoids on the erythrocyte surface is closely associated with the wider problem of the mode of entry of viruses into cells and useful materials and data have been passed on to Dr. Chu, of the London School of Hygiene and Tropical Medicine, who is studying this aspect of virus infections.

Toxins and Enzymes. Dr. M. Macfarlane has studied the lecithinase present in culture filtrates of *Cl. œdematiens* Type A and Type B. It has been found, by isolation of the hydrolysis products, that these enzymes are similar in their biochemical action to *Cl. welchii* lecithinase, but that the three enzymes are immunologically distinct from each other. *Cl. hæmolyticum* toxin also contains a lecithinase, which is probably the main lethal component and is antigenically similar to *Cl. œdematiens* Type B lecithinase.

The establishment of the identity of biochemical action of lecithinases which are immunologically distinct is being exploited by investigating, in the hæmolytic system, the mutual effect of type-specific groups in the bacterial enzyme and species-specific groups in the red-cell on the actual degree of hæmolysis produced by nominally equal amounts of the enzymes. The striking differences observed in these relatively simple "host-parasite" systems seems pertinent to the general problem of virulence.

Dr. Macfarlane has also resumed work on the enzymic activity of viruses which was interrupted in 1939.

Bacterial Antigens. Mr. K. A. Smith and Dr. Morgan are attempting to devise new methods for the isolation of the O-somatic antigen of *Shigella dysenteriæ* which will yield a homogeneous antigenic complex suitable for step-wise degradation, for if any significance is to be attached to the isolation of certain substances in small yield the purity of the antigenic complex is of prime importance. The identification of the prosthetic group of the conjugated protein component of the antigenic complex is the immediate task.

Dr. Morgan and Dr. Feinberg have now collected a sufficient quantity of *Trichomonas fœtus* to enable the preliminary observations concerning the nature of its antigenic complex to be repeated and extended. The immunological aspects of the work are being developed by Dr. M. Robertson.

Gramicidin and related peptides. While at Fysikalisk-Kemiska Institutionen, Uppsala, Dr. Synge, in collaboration with Dr. K. O. Pedersen, carried out some diffusion measurements on these substances. Since returning, Dr. Synge has continued studies of gramicidin. New stoichiometric data have been obtained, which in conjunction with new crystallographic data of Dr. Crowfoot, Oxford, and the above-mentioned diffusion studies, have led to a revised picture of the over-all composition of the gramicidin molecule. Further studies of partial hydrolysates of gramicidin have led to the identification of various peptides. Work begun at Uppsala on new techniques for separating such peptides is being continued. Special attention has been paid to optical inversion in this work and an ultra-micro procedure, making use of D-amino acid oxidase from the kidney has been developed for determining the optical character of amino-acids.

Dr. A. T. James is studying non-peptide linkages in gramicidin and associated problems concerning the mode of incorporation of the ethanolamine residues.

The Institute has acquired during the past year a Tiselius-Claesson interferometric apparatus for adsorption analysis and general use in chromatographic work.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Blood Clotting Factors. Dr. Paul Owren has obtained more purified preparations of Factor V from bovine plasma by a method involving precipitation by ether at low temperature with control of pH and ionic strength.

Mr. J. W. Lyttleton has examined the purification of human thrombin by ether precipitation, and has been able to improve the stability and purity of the thrombin by the removal of contaminating serum protease. Preliminary studies have also been made on the purification of bovine fibrinogen by precipitation with ether at low temperature.

Tetanus Toxin and Antitoxin. Mr. Cinader has continued his studies on the interaction of tetanus toxin and antitoxin in collaboration with Dr. Weitz. Flocculation values have been distinguished by the aid of absorption tests; L +/Lf values, dilution ratios and mouse-guinea pig ratios have been determined for a series of sera taken during the course of immunisation, for several hyperimmune antitoxins and for the isolated β- and γ-globulins from the sera. The γ-globulin appears to have a higher L+/Lf ratio, to flocculate faster and to be more avid than β-globulin as measured by both animal tests.

Ultrasonic Vibrations and the Protein Molecules. Mr. C. J. B. Bradish has been examining the effects of ultrasonic vibration on various proteins in aqueous solution, with particular reference to the dissociation reaction of the hemocyanin of Helix Pomatia. These experiments have been controlled by measurements with the ultracentrifuge. Some attention has been paid to the design of a suitable cell for use in irradiation and to the measurement of the energy density of the ultrasonic radiation.

In collaboration with Dr. M. Robertson and Dr. Feinberg a soluble antigen has been obtained by the ultrasonic irradiation of saline suspensions of *Trichomonas fœtus.*

Electrophoresis of Sera. In collaboration with Dr. C. H. Gray (King's College Hospital), Dr. R. A. Kekwick has examined a group of sera from patients with differing types of jaundice. It has been established that a small but definite fraction of the bilirubin migrates with the α-globulin in addition to the bulk of the bilirubin which migrates with the albumin. It was further demonstrated that the binding of the bilirubin by differing plasma proteins bears no relationship to the nature of the direct Van den Bergh reaction.

The distribution of human plasma proteins in malnutrition has been determined on a large group of sera obtained from cases of malnutrition in Germany. This forms a part of an extensive general survey being carried out by Professor R. A. McCance and Miss E. M. Widdowson (Dept. of Experimental Medicine, Cambridge).

Facilities have been extended to Dr. Nicholas Martin (St. George's Hospital), for the electrophoretic examination of pathological human sera.

Fœtal and Maternal Blood. In collaboration with Dr. W. Godden and Dr. A. Dalgarno of the Rowett Institute, Dr. E. F. McCarthy has continued his electrophoretic investigations on sera from pregnant ewes, their fœtuses and lambs. Osmotic pressure measurements have been made on protein fractions obtained from the sera.

Human Plasma and Plasma Products. During the year the Unit administered by the Medical Research Council on behalf of the Ministry of Health has tested and prepared 20,000 bottles of dried human plasma for issue to hospitals. The production and distribution of fibrinogen, fibrin foam and thrombin has continued and 2,400 bottles of fibrinogen, 5,000 bottles of fibrin foam, and 500,000 units of thrombin have been made for clinical use.

Miss B. Balfour has undertaken the bacteriology for the Unit and is investigating the characteristics of a coliform organism isolated from plasma which grows freely at 3°C. and will coagulate plasma at room temperature.

Dr. Mackay and Dr. Kekwick have continued their work on the ether fractionation of plasma proteins. A method for the separation of β- and γ-globulin has been devised and the bacterial, virus and blood group antibodies in the different fractions have been assayed. A method for the preparation of an albumin fraction to be used in serological work is also being investigated.

NUTRITIONAL STUDIES.

Synthetic diets for rats. During 1947 Miss A. M. Copping and Miss V. R. G. Pond have continued their investigation of complete synthetic diets for rats. It is now clear from the results that some factor other than the known members of the vitamin B complex is required for normal growth, but the research on this point has been seriously hampered by lack of supplies of purified casein.

Biological estimation of Riboflavin. A co-operative experiment was undertaken on behalf of the Vitamin B Sub-Committee with Dr. Coward of the Pharmaceutical Society and Dr. Kon of the National Institute for Research in Dairying in order to study the biological method of estimating riboflavin in cereals. A satisfactory result has been obtained.

In connection with human metabolism studies being made by Professor McCance and his colleagues of the Medical Research Council Unit at Wuppertal Elberfeld (British Zone, Germany) samples of breads have been tested biologically for the riboflavin content for comparison with microbiological estimations made at Wuppertal.

Effect of vitamins on Gastric conditions. Miss E. M. Hume, with the assistance of Miss H. Henderson Smith, has continued her studies of vitamin A and vitamin D in relation to the stomach, in both rats and human beings.

A study is being made of human subjects with peptic ulceration diagnosed radiographically, or who have pain without ulceration though they may or may not at some previous time have had proved ulceration. Some preliminary studies were at first made on out-patients at the Royal Free Hospital with satisfactory results. More recently subjects have been obtained through the co-operation of the Medical Service of the Post Office. Dr. Roberts, the senior Medical Officer, has permitted Dr. V. C. Medvei of the Medical Branch of Mount Pleasant to collaborate in the research. The completeness of the records and the continuity of the service allow the cases to be followed up indefinitely if desired. The results already obtained confirm the claim of others that great benefit can be conferred in certain cases. Treatment with vitamin A has had no consistent effect on the gastric acidity. In this work Miss Hume has had the assistance of Miss Pond and the staffs of various departments of the Royal Free Hospital.

In cases where vitamin A treatment has been unsuccessful, it is intended to try treatment with moderate doses of vitamin D.

In the experiments with rats deprived of vitamin A, the difficulty of finding again the factor which was present in the partly purified casein used in the earlier experiments, and which prevented proliferation of the gastric epithelium, has not been wholly overcome. The factor appeared to be present in unpurified casein but is not the same as a factor in certain liver fractions. These fractions do, however, contain a factor which is necessary for the growth of rats, which is removed from casein on purification, and which is not present in dried brewer's yeast. It is of practical importance that a convenient source of this factor should be found for inclusion in synthetic diets for experiments of all kinds in which purified casein is used.

The biosynthesis of nicotinamide by the intestinal bacteria. Dr. P. Ellinger, in collaboration with Mr. Abdel Kader and Dr. Emanuelowa, studied the influence of a number of amino acids added to an ammonium lactate medium on the production of nicotinamide by a number of strains of *B.coli in vitro*. Of all amino acids examined only ornithine increased the formation of nicotinamide up to 10 times and arginine and glutamine to a lesser degree.

Tryptophan as precursor of nicotinamide. Dr. Ellinger and Mr. Abdel Kader continued their investigations on this subject. In rats tryptophan produced a far greater increase of the nicotinamide methochloride elimination after oral than after intraperitoneal administration. This increase of nicotinamide methochloride elimination by tryotophan was considerably reduced after application of "sterilising" drugs to the animals. Both facts suggest the participation of the intestinal flora in the biosynthesis of nicotinamide from tryptophan. Tryptophan has no effect on the biosynthesis of nicotinamide by pure cultures of *B.coli*. In mixed cultures from cæcum contents, however, tryptophan increases the nicotinamide formation *in vitro*.

Metabolism of nicotinamide in various mammalian species. Dr. Ellinger and Mr. Abdel Kader investigated the metabolism of nicotinamide, nicotinic acid and nikethamide in man, dog, cat, rat, rabbit and guinea pig. They found that nicotinic acid was aminated by man, dog, cat and rat and nicotinamide de-aminated by rabbit and guinea pig. All species but guinea pig methylated the metabolites to nicotinamide methochloride or trigonelline. Rabbit and guinea pig were found to eliminate a hitherto unknown metabolite in very minute amounts and from rabbit's urine a new purplish blue fluorescent pigment was isolated after ingestion of nikethamide.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Bacteriological Studies. Sir Paul Fildes has been studying the synthesis of tryptophan by *Bact. typhosum* as a mutational phenomenon and with Mr. D. Kay is working on typhoid bacterial viruses.

Dr. G. P. Gladstone has worked out a method for producing cell-free anthrax vaccine of high potency. He is investigating the importance of methionine and vitamin B in the nutrition of *Bact. typhosum* in overoxygenated cultures.

Dr. M. R. Pollock has continued his work on the growth requirement of *H. pertussis* and the action of long chain unsaturated fatty acids upon micro-organisms in general. A study of the mechanism of enzyme adaptation in bacterial cell suspensions, in collaboration with Mr. S. D. Wainwright, is also proceeding.

Dr. D. Herbert and Miss J. Pinsent are continuing their work on bacterial enzymes and are studying the effects of iron on the growth and enzymic make-up of bacteria.

Dr. G. A. Howard has isolated the unsaturated fatty acid which is produced by *H. pertussis* and causes inhibition of its growth.

Dr. A. M. Staub continues the serological analysis of the anthrax antigen.

Miss B. Boughton is preparing derivatives of anthranilic acid with the object of finding inhibitors of tryptophan synthesis.

Miss R. M. M. Jordan is investigating the growth requirements of *Past. septica* and the use of cell-free culture filtrates as a protective vaccine.

Mr. G. H. Smith has isolated pure tryptophan from *Bact. typhosum* and is following the biosynthesis of tryptophan by isotopically marked compounds.

Nutritional Studies. Dr. S. S. Zilva, in collaboration with Mr. H. A. Painter, has submitted to a detailed scrutiny the observations made by some American workers that an excess of *l*-ascorbic acid is necessary in order to break down fully aromatic amino acids in the body. They could not obtain any evidence that such an excess is necessary for normal utilisation of these products of protein degradation but found that an excess of vitamin C is required to break down fully the aromatic part of these compounds only when they are consumed in abnormally high quantities. In the absence of *l*-ascorbic acid there is then an accumulation of the hydroxyphenyl compounds in the cæcum which passes into the blood stream raising the concentration beyond a level consistent with their normal breakdown. This level can be raised to some extent when excessive quantities of vitamin C are circulating in the blood. It is assumed that the accumulation of the hydroxyphenyl compounds in the large intestine is due to a change in the intestinal flora or in its action on these compounds and is brought about by the absence of *l*-ascorbic acid from the diet. Bactericidal agents produce a similar effect.

In connection with the above investigation Dr. Zilva and Mr. Painter made a series of observations of theoretical interest which led to the conclusion that *p*-hydroxyphenylpyruvic acid undergoes in aqueous solution a certain tautomeric change and that this change proceeds differently in urine and in animal tissues.

Blood Group Studies. The work of this Unit under Dr. Race has been mainly devoted to the Rh blood groups. Numerous rare allelomorphs at the D locus have been identified and two more allelomorphs at the C-c-C^w locus called c^v and C^u have been established.

Under Dr. Lawler the blood grouping of families with rare inherited diseases progresses. This is a long term investigation done in the hope of detecting genetic linkage, if it exists, between the disease genes and one of the blood group genes.

The work of Miss Sanger has resulted in the splitting of the MN blood groups. There are now six recognisable groups on this system, instead of three.

The Unit works in close collaboration with the Ministry of Health Blood Group Reference Laboratory.

National Collection of Type Cultures. The year was one of re-organisation and a start was made to bring the Collection into line with the Medical Research Council's intention that its activities should be confined to maintaining cultures of medical and veterinary interest. Arrangements were made for the transfer of the fungi to the Commonwealth Mycological Institute and this was completed by the end of the year.

The Collection now consists of about 3,000 strains of bacteria and these are being checked for purity. About 200 new strains were added; some were new species, others were to replace old strains that had become atypical. Over 8,000 cultures were distributed during the year.

A *List of Species* maintained in the Collection was prepared and will be published during 1948 by H.M. Stationery Office.

MINISTRY OF HEALTH

Blood Group Reference Laboratory. During 1947 this unit examined 8,700 tubes and 3,500 bottles of serum for suitability for blood grouping serum. 75 litres of grouping serum were issued.

Full Rh genotyping tests were carried out on 2,230 specimens of blood, and 1,070 specimens of serum were tested for anti-Rh and other abnormal antibodies. Supplies of anti-Rh and other special grouping sera were obtained from human donors and from immunised rabbits. One litre of such sera was distributed.

Investigations were carried out on newly discovered blood group antigens and full blood group tests performed on groups of natives of a number of foreign countries and especially on the Basques.

In conjunction with the Blood Products Unit of the Medical Research Council and the National Institute for Medical Research, the first stages in the preparation of International Standard anti-A and anti-B grouping sera have been carried out.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the Director and all his co-workers of the scientific, administrative and technical staffs have worked together during the period under review.

H. H. DALE,

Chairman of the Governing Body.

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.

CHICK, H. ... ... NOTE ON METHODS OF DETERMINING THE NUTRITIVE VALUE OF PROTEINS. *Chemistry and Industry*, No. 23, 1947.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1948.

FINANCIAL REPORT OF THE GOVERNING BODY.

1. The Balance Sheet for the year ended 31st December 1948 shows balances to the credit of the various funds as follows: Capital Fund £697,199; Specific Funds £111,711; Contingency Reserve £70,778 and Bequest Funds £17,700.

2. Conversion of the Institute's General Fund and Jenner Memorial Studentship Fund holdings of railway stocks into British Transport 3% Guaranteed Stock 1978/88 showed a book profit of £1,624 and a loss of £754 respectively. The General Fund holdings had however been severely written down in the past.

3. Income and Expenditure Accounts show the income for the year as £106,114 compared with £82,651 in 1947. Expenditure amounted to £82,366 against £92,160 last year. Decreases in Serum, Vaccine and Vaccine Lymph Expenses, Animal House Expenses and Forage, Buildings and Alterations and General Apparatus and New Installations with increases in Gas, Water, Fuel & Electricity and Biochemical Expenses accounted for much of the difference.

4. The year's surplus of £23,748 shown by the General Fund Income and Expenditure account has been transferred to the Contingency Reserve.

5. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £8,020, £4,631 and £1,482 respectively.

6. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

H. H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

26th April, 1949.

BALANCE SHEET

(1947) £		£	£	£
	Capital Fund:—			
	Donations, &c., received to date from the following:—			
2,000	Dr. Ludwig Mond (1893)		2,000	
46,380	Berridge Trustees (1893/98)		46,380	
10,000	Worshipful Company of Grocers' (1894)		10,000	
250,000	Lord Iveagh (1900)		250,000	
18,904	Lord Lister's Bequest (1913/23)		18,904	
7,114	William Henry Clarke Bequest (1923/6)		7,114	
3,400	Rockefeller Foundation (1935/6)		3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)		500	
21,097	Other Donations and Legacies (1891-1938)		21,097	
	General Fund Income and Expenditure Account Accumulated Surpluses as at 31st December, 1947	336,180		
	Add Surplus on Investments Converted	1,624		
336,180			337,804	
695,575				697,199
	Specific Funds:—			
72,171	Sinking Fund for Freehold Buildings		75,015	
36,300	Pension Fund		36,696	
108,471				111,711
	Contingency Reserve:—			
	As at 31st December 1947		47,030	
	Add Surplus on General Fund Income and Expenditure Account, 1948		23,748	
47,030				70,778
851,076				879,688
	Current Liabilities:—			
15,904	Creditors and accrued charges		12,224	
672	Balance of Cancer Research Legacy (1937)		672	
16,576				12,896
867,652				892,584
	Bequest Funds:—			
10,179	Jenner Memorial Studentship Fund		9,476	
	Morna Macleod Scholarship Fund:—			
	Isobel S. Macleod Bequest	1,500		
	William A. Macleod Bequest	5,966		
	Interest on Investments	260		
6,750			7,726	
672	Bacot Bequest Fund		498	
17,601				17,700
£885,253				£910,284

H. H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have obtained all the information and explanations which to the best of our knowledge and belief were far as appears from our examination of those books. We have examined the above Balance Sheet and annexed amount of £8,010 due from a foreign Government which has not been agreed and which may be partly irrecovergiven to us the said accounts (amplified by the information given in paragraph 5 of the Financial Report of the Gov-Sheet gives a true and fair view of the state of the Institute's affairs as at 31st December, 1948, and the Income and

London, 29th April, 1949.

31st DECEMBER, 1948.

(1947) £		£	£	£
	Fixed Assets:—			
	FREEHOLD PROPERTY at cost:			
73,717	Land and Buildings, Chelsea	73,717		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,222	
	(*Note: Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	LEASEHOLD PROPERTY:—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,383		
351			286	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
99,045	(*Note: Additions and replacements since 31st December, 1920 have been charged to Revenue*)		—	98,980

Quoted Investments and Uninvested Cash relating to General and Specific Funds:—

		Quoted Investments at cost less amounts written off	Uninvested Cash		
606,343	General Fund	608,562		608,562	
72,171	Sinking Fund for Freehold Buildings ..	74,954	61	75,015	
36,300	Pension Fund	35,544	1,152	36,696	
714,814		719,060	1,213	720,273	720,273

(*Market Value of Investments on London Stock Exchange £796,540*)

	Current Assets:—			
38,902	Debtors and Payments in advance		32,809	
14,891	Cash at Bankers and in hand		40,522	
53,793				73,331
867,652				892,584

(*Note: See paragraph 5 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts*).

Quoted Investments and Uninvested Cash relating to Bequest Funds:—

		Quoted Investments at cost	Uninvested Cash		
10,179	Jenner Memorial Studentship Fund	8,545	931	9,476	
6,750	Morna Macleod Scholarship Fund	7,606	120	7,726	
672	Bacot Bequest Fund	—	498	498	
17,601		16,151	1,549	17,700	17,700

(*Market Value of Investments on London Stock Exchange £15,983*)

£885,253	£910,284

TO THE MEMBERS.

necessary for the purposes of our audit. In our opinion proper books of account have been kept by the Institute so Income and Expenditure Accounts which are in agreement with the books of account. Debtors include an able. Subject to this remark in our opinion and to the best of our information and according to the explanations erning Body) give the information required by the Companies Act, 1948, in the manner so required and the Balance Expenditure Account of the General Fund gives a true and fair view of the surplus for the year ended on that date.

COOPER BROTHERS & CO., *Chartered Accountants.* } *Auditors.*

INCOME AND EXPENDITURE ACCOUNTS

General

(1947) £		£
39,884	Salaries and Wages	40,241
1,781	Premiums on Federated Superannuation Policies	1,535
1,676	Rent, Rates and Insurance	1,959
3,722	Gas, Water, Fuel and Electricity	4,341
556	Stationery, Printing and Postage	468
515	Office Expenses and Donations	437
136	Auditors' Fee	136
360	Travelling Expenses	340
815	Biochemical Expenses	1,740
480	Bacteriological and Experimental Pathology Expenses	541
318	Nutrition Expenses	399
493	Biophysics Expenses	597
14,247	Serum, Vaccine and Vaccine Lymph Expenses	11,657
3,549	Animals	3,951
5,880	Animal House Expenses and Forage	4,569
12,898	Buildings, Alterations, Repairs and Renewals	4,792
1,336	General Apparatus and New Installations	685
474	Library Expenses	623
287	General Stores	446
65	Amount written off Leasehold Property	65
2,738	Amount transferred to Sinking Fund for Freehold Buildings (including £2,420 Interest on Investments)	2,844
—	*Surplus* transferred to Contingency Reserve	23,748
£92,160		£106,114

Pension

£		£
1,089	Pensions	1,210
517	Balance added to Fund	396
£1,606		£1,606

Jenner Memorial

£		£
300	Stipend of Student	250
—	Deficit on conversion of Investment	754
10	Balance added to Fund (1947)	—
£310		£1,004

Morna Macleod

£		£
45	Balance added to Fund	215
45		£215

Bacot

£		£
—	Purchase of Furniture	195
21	Balance added to Fund (1947)	—
£21		£195

for the year ended 31st December, 1948.

Fund.

(1947) £		£	£
	Interest and Dividends (gross):		
21,981	General Fund Investments	21,362	
2,314	Sinking Fund Investments	2,420	
			23,782
53,514	Sales of Sera, Vaccines, Vaccine Lymph, &c.		75,527
4,842	Rent		6,805
9,509	*Deficit* transferred to Contingency Reserve (1947)		—
£92,160			£106,114

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
£1,606		£1,606

Studentship Fund.

£		£
310	Interest on Investments (gross)	300
—	Balance Deducted from Fund	704
£310		£1,004

Scholarship Fund.

£		£
45	Interest on Investments (gross)	215
45		£215

Bequest Fund.

£		£
21	Interest on Investment (gross)	21
—	Balance deducted from Fund	174
£21		£195

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,

1949.

Chelsea Bridge Road,
London, S.W. 1.

June 15th. 1949.

THE GOVERNING BODY.

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S., *Hon. Treasurer.*
PROFESSOR S. P. BEDSON, M.D., B.S., F.R.C.P., D.Sc., F.R.S.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.
DR. A. N. DRURY, C.B.E., M.A., M.D., F.R.S.
SIR PAUL FILDES, O.B.E., M.A., M.B., B.Ch., D.Sc., F.R.S.
THE EARL OF IVEAGH, C.B., C.M.G.

THE COUNCIL.

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PROFESSOR F. W. ROGERS BRAMBELL, B.A., D.Sc.	Royal Irish Academy.
THE PRESIDENT OF THE ROYAL COLLEGE OF VETERINARY SURGEONS	Royal College of Veterinary Surgeons.
PROFESSOR H. R. DEAN, M.D., F.R.C.P., LL.D.	University of Cambridge.
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V. ZACHARY COPE, M.S., F.R.C.S.	British Medical Association.
PROFESSOR JOHN A. RYLE, M.D., F.R.C.P.	Members of the Institute.
THE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS ...	Royal College of Surgeons of England.
PROFESSOR R. A. PETERS, M.D., F.R.S.	Members of the Institute.
PROFESSOR H. B. MAITLAND, M.D., M.R.C.S., L.R.C.P. ...	Victoria University of Manchester.
PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.S., F.R.S.	Members of the Institute.
SIR HENRY DALE, O.M., G.B.E., M.D. F.R.C.P., F.R.S. ...	" "
PROFESSOR SIR HOWARD W. FLOREY, M.A., PH.D., M.B., B.S., F.R.S.	University of Oxford.
PROFESSOR G. S. WILSON, M.D., B.S., F.R.C.P.	University of London.
SIR WILLIAM C. DAMPIER, Sc.D., F.R.S.	Royal Agricultural Society.
SIR WILLIAM WILSON JAMESON, K.C.B., M.D., F.R.C.P., LL.D.	Members of the Institute.
PROFESSOR A. V. HILL, C.H., F.R.S.	" "
PROFESSOR H. S. RAPER, C.B.E., D.Sc., F.R.S.	" "
A. N. DRURY, C.B.E., M.A., M.D., F.R.S.	" "
SIR EDWARD MELLANBY, K.C.B., M.D., F.R.S.	" "
HARRIETTE CHICK, C.B.E., D.Sc.	" "
SIR JOHN ANDERSON, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., B.Sc., LL.D., F.R.S.	" "
THE EARL OF IVEAGH, C.B., C.M.G.	" "
PROFESSOR S. R. K. GLANVILLE, M.A., F.S.A.	Worshipful Company of Grocers.
MAJOR L. M. E. DENT, D.S.O.	" "
PROFESSOR J. W. BIGGER, M.D., Sc.D., F.R.C.P.	University of Dublin.
THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS ...	Royal College of Physicians, London.
SIR CHARLES J. MARTIN, C.M.G., M.B., LL.D., F.R.S. ...	Members of the Institute.
LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.	" "
PROFESSOR M. GREENWOOD, D.Sc., F.R.C.P., F.R.S. ...	" "
SIR CHARLES HARINGTON, M.A., PH.D., F.R.S.	" "
SIR PAUL FILDES, O.B.E., M.A., M.B., B.CH., D.Sc., F.R.S.	" "
SIR PERCIVAL HARTLEY, C.B.E., D.Sc., F.R.S.	" "
J. HENDERSON SMITH, M.B., B.CH.	" "
PROFESSOR M. J. STEWART, M.B., F.R.C.P., LL.D. ...	" "

THE STAFF.

DIRECTOR:

*Alan N. Drury, C.B.E., M.A., M.D., F.R.S.

BACTERIOLOGY, SEROLOGY, and EXPERIMENTAL PATHOLOGY.

*A. N. Drury, C.B.E., M.A., M.D., F.R.S.
Muriel Robertson, M.A., D.Sc., LL.D., F.R.S. (*Honorary*)
Emmy Klieneberger-Nobel, Ph.D., D.Sc.
Ruth G. Wittler, M.Sc., Ph.D. (*Jenner Memorial Research Student*).
Jane Clausen, B.Sc. (*Medical Research Council Student*).

BIOCHEMISTRY AND IMMUNOCHEMISTRY.

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S. (*Reader in Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
Marjorie G. Macfarlane, D.Sc., Ph.D.
P. Ellinger, Dr. Phil. and Med., F.R.I.C. (*Grantee*)
A. T. James, B.Sc., Ph.D. (*Beit Memorial Research Fellow*).
D. Aminoff, B.Sc., (*Research Student*).
J. D. Feinberg, M.S., Dr. V. M. (*U.S.A.*).
E. F. Annison, B.Sc. (*Medical Research Council Student*).
J. F. McCrea, M.A.Sc., Ph.D. (*Australia*).
W. Mosimann, D.Phil. (*Switzerland*).

NUTRITION.

*Harriette Chick, C.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).
Alice M. Copping, M.Sc.
Hannah Henderson Smith.

Medical Research Council External Scientific Staff:

*S. S. Zilva, D.Sc., Ph.D., F.R.I.C. (*Honorary*).
H. A. Painter, B.Sc., Ph.D., A.R.I.C.
H. R. Perkins, B.Sc.

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
E. F. McCarthy, M.B., B.Ch., M.Sc. (*Medical Research Council of Ireland*).
J. W. Lyttleton, M.Sc. (*Beit Memorial Research Fellow*).
G. Hamoir, D.Chem. (*Belgium*).

Blood Products Research Unit.

Medical Research Council External Scientific Staff:

Margaret E. Mackay, M.Sc., Ph.D.
Noreen M. E. Haysom, B.Sc.
Margaret Nance, B.Sc.
H. R. F. Arnstein, B.Sc.
E. A. McCulloch, M.D. *Ellen Mickle Fellow, University of Toronto.*

PREPARATION AND STUDY OF THERAPEUTIC SERA.

W. d'A. Maycock, M.B.E., M.D., *Superintendent of Elstree Laboratories and Estate.*
G. F. B. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc.

PREPARATION AND STUDY OF VACCINE LYMPH.

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.B., B.S.

PREPARATION AND STUDY OF BACTERIAL VACCINES.

A. F. B. Standfast, M.A., Dip.Bact.
Margaret P. D. Pile, B.Sc.

†*Appointed Teacher of the University of London.* **Recognised Teacher of the University of London.*

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Bacterial Chemistry Unit.

M. R. Pollock, B.A., M.B., B.Ch. (*Leverhulme Research Fellow*).
D. Herbert, M.A., Ph.D. (*Leverhulme Research Fellow*).
A. J. P. Martin, M.A., Ph.D.
Barbara Boughton, B.Sc. (*Leverhulme Research Student*).
Jane Pinsent, B.A. (*Leverhulme Research Student*).
G. H. Smith, B.Sc. (*Leverhulme Research Student*).
S. D. Wainwright, B.A. (*Leverhulme Research Student*).

National Collection of Type Cultures.

S. T. Cowan, M.D., Dip. Bact., (*Curator*).
Constance Shaw, M.Sc., Dip. Bact.
Mabel Rhodes.
Mary G. Jennens, B.Sc.

Blood Group Research Unit.

R. R. Race, Ph.D., M.R.C.S., L.R.C.P.
Sylvia Lawler, M.B., B.S. (*Research Student*).
Doreen Bertinshaw, B.Sc.
Helene Holt, B.A.

MINISTRY OF HEALTH.

Blood Group Reference Laboratory.

A. E. Mourant, D.M., M.A., D.Phil.
Elizabeth W. Ikin, B.Sc.
Joy Donegani, B.Sc.

ADMINISTRATION.

Secretary	A. L. White.
Elstree Secretary and Estate Manager	F. K. Fox.
Assistant Secretary and Accountant	S. A. White, A.A.C.C.A.

Solicitor:

Field, Roscoe & Co.,
52, Bedford Square, W.C. 1.

Auditors:

Cooper Brothers & Co.,
14, George Street, Mansion House, E.C. 4.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 15th. 1949.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report on the work of the Institute for the year 1948/9.

GOVERNING BODY.

It is announced with great regret that Lord Horder, owing to the increase of other demands upon his time felt compelled to resign his seat on the Board on which he had served for fourteen years. At a meeting held on January 19th, 1949, the following resolution of appreciation of his services was recorded :—

> "That the Governing Body learned with regret that the increase of other demands on his time had obliged Lord Horder to retire from membership of their Body. They recalled that Lord Horder on the nomination first of the late Lord Moyne and subsequently of the present Lord Iveagh, had served on the Governing Body for fourteen years, and for longer, indeed, than any other Governor at the date of his retirement. In accepting Lord Horder's resignation with great regret, they desired to record their grateful sense of the constant interest which he had shown in the affairs of the Institute and of the value to their deliberations of his wise counsel."

As successor to Lord Horder, Lord Iveagh has appointed Dr. A. N. Drury as one of his representatives on the Governing Body.

The Council at its last meeting re-elected Professor H. R. Dean, Sir Paul Fildes and Sir Henry H. Dale as its representatives on the Governing Body until December 31st, 1949.

In accordance with the provisions contained in Section 185 of the Companies Act, 1948, the Governing Body will, before the Annual General Meeting, convene an Extraordinary General Meeting of the members when a resolution will be proposed for the purpose of altering the Articles of Association by the insertion of a new Article to withdraw the Institute from the scope of sub-sections 1 to 6 of Section 185 of the Act, which deal with the appointment of company directors of 70 years of age or over.

During the year the Institute, being a recognised School of the University of London, received a statutory visit of inspection from the Principal and appointed Inspectors of the University. Certain recommendations were made with which the Governing Body wish to conform and as these will affect the constitution of the Governing Body the members will in due course be asked to approve alterations to the Institute's Memorandum of Association for this purpose.

COUNCIL.

At last year's Annual General Meeting, the three retiring members of Council, Sir Charles Martin, Lord Horder and Professor M. Greenwood were re-elected.

The three members due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Sir Charles Harington, Sir Paul Fildes and Sir Percival Hartley, each a representative of the Members of the Institute.

MEMBERS.

The Governing Body records with regret the deaths during the year of Dr. G. L. L. Lawson, Dr. Marjory Stephenson and Dr. C. M. Wenyon.

STAFF.

The Governing Body take pleasure in recording the election of Dr. W. T. J. Morgan to the Fellowship of the Royal Society.

Dr. E. S. Duthie resigned on November 30th to take up an appointment as Assistant Director of Pathology, Southampton General Hospital. Dr. W. d'A. Maycock has been appointed Superintendent of the Elstree Laboratories and Estate.

Dr. R. L. M. Synge resigned in September on taking up a post at the Rowett Research Institute, and Dr. E. L. McCarthy, on taking up a Fellowship of the Medical Research Council of Ireland resigned in September, but has continued to work at the Institute since that date.

Mr. M. Stack left the service of the Institute in September on receiving an appointment at Guy's Hospital Medical School.

Dr. C. J. Bradish resigned his Studentship in November and has joined the research staff of the Foot and Mouth Disease Research Station at Pirbright.

Miss S. J. L. Spooner and Mr. K. A. Smith on the completion of the tenure of their Studentships joined the research staff of the Chester Beatty Institute attached to the Royal Cancer Hospital.

Mr. B. Cinader, on the invitation of Professor Pillemer, of the department of Pathology, Western Reserve University, Cleveland, U.S.A., has taken up a year's studentship there and Miss Ruth Wittler from that University has been appointed to a Research Studentship of the Institute.

The Bacterial Chemistry Unit, under the direction of Sir Paul Fildes until his retirement in March, the Blood Products Research Unit and the Blood Group Research Unit of the Medical Research Council are still accommodated at the Institute, as is also the Blood Group Reference Laboratory of the Ministry of Health.

The Governing Body, before surveying the scientific work carried out during the year, once again desires to record its appreciation of the continued co-operation and collaboration of the Medical Research Council with the Institute.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus Pertussis. Mr. A. F. B. Standfast has continued his work on the factors involved in the virulence of *H. pertussis* for mice and the influence of these factors on the immunizing properties of whooping cough vaccines. From the results so far obtained it would appear that the factors involved in high virulence are not the same as those necessary for the production of high potency vaccines.

The investigation of Kendrick's mouse test for potency of vaccines has been completed and the results are being analysed statistically by Dr. J. O. Irwin (London School of Hygiene and Tropical Medicine).

V. Choleræ. Miss M. P. D. Pile has started an investigation on the part played by cholera enzymes, such as the mucinase, on the potency of cholera vaccines.

Trichomonas Studies. Work on trichomoniasis in cattle has been continued by Dr. M. Robertson in collaboration with Dr. W. R. Kerr (Veterinary Research Dept., Ministry of Agriculture, Northern Ireland).

The desensitisation studies have shown that temporary desensitisation of the skin of sensitised animals takes place specifically by further absorption of appropriate doses of antigen and non-specifically by parturition, upon injection of adrenal cortical hormone (C-11 oxygenated adrenal cortical hormone) and after injection of sphingomyelin.

The differential white cell counts during these various conditions have been followed and a correlation between desensitisation and a characteristic leucopenia usually, but not always, accompanied by a rise in neutrophil cells has been observed. It is concluded that the white cell picture in all these cases is related to the mobilisation of the pituitary cortical hormone complex and the desensitisation follows as one of the results.

The reaction of the white corpuscles of the blood to the injection of antigen during the course of immunisation is now being studied. An investigation is being carried out into the site of the non-specific agglutinin and the specific immune body in the different serum fractions with the co-operation of the department of Biophysics.

Acknowledgment is due to the Agricultural Research Council for a grant to Dr. Robertson which has enabled this work to be undertaken.

Vaccine Lymph. Dr. D. McClean has investigated the action of "Roccal" (a quarternary ammonium detergent) on the bacterial contamination of crude vaccine pulp. The use of this antiseptic was advocated by Ducor and it is employed in some laboratories in America. Dr. McClean has found that, when added to vaccine pulp, it acts as a bacteriostatic rather than a bactericidal agent and it is, of course, ineffective against *Ps. pyocyanea.* When "Roccal" is used as a spray on the vaccinated area during incubation it materially reduces the yield of vaccine pulp. It does not appear to possess any advantages over phenol in the rapid purification of vaccine lymph.

Dr. L. H. Collier has been investigating methods of preserving vaccinia virus without the use of refrigeration. Preliminary experiments showed that desiccation of crude vaccine pulp according to the method of Otten, with subsequent storage *in vacuo* at temperatures of 0°-4°C., 22°C. and 37°C. did not result in a stable product. Material prepared in this way showed a complete loss of potency when held at 22°C. and 37°C. for eight weeks, and considerable diminution in potency when kept at 0° - 4°C. for this period. Work is now complete on the production of highly purified elementary body suspensions for use in subsequent experiments of this type, in which the virus will be dried from the frozen state.

With the object of producing a sterile vaccine capable of immunizing against smallpox when injected intracutaneously, Dr. McClean has adapted a strain of vaccinia to grow readily in the dermis. Dr. Collier is investigating the behaviour of this strain when propagated in eggs.

Experiments on the action of certain detergents on vaccinia virus have been commenced.

Bacterial Cytology. Dr. Klieneberger-Nobel has carried out an investigation on the origin of the L-forms in bacterial cultures with some of the newer cytological methods. As a result of these observations she has abandoned the symbiosis theory and has formed the new conception that bacteria exist in an A-stage (bacterial stage) and an L-stage (pleomorphic, amorphous stage).

Plasma Substitutes. Dr. W. d'A. Maycock and Miss S. J. L. Spooner have continued work on dextran, the main concern being the study of the distribution of injected dextran in the tissues, using for its detection an antiserum to *Leuconostoc Mesenteroides,* with which degraded dextran apparently reacts as a haptene. Dextran, as prepared for infusion, has been detected in all tissues examined up to eight weeks following injection into rabbits in doses of 9 gms./Kilo. After 16 weeks it was still detectable in the brain, bone marrow and skin, but not in other tissues.

Experiments designed to study the urinary excretion of various batches of refined dextran, prepared by acetone fractionation, have been performed in conjunction with Dr. C. Ricketts (Medical Research Council Burns Unit).

In November Dr. Maycock visited America and Canada on behalf of the Medical Research Council to investigate the use of ultra-violet light for the sterilization of plasma.

Slow constrictor substance in human plasma. Dr. A. N. Drury, Dr. M. E. Mackay and Miss Spooner have been investigating the substance which is present in human plasma or serum which gives rise to a slow constriction of the guinea pig's gut. When the serum is fractionated with ether, the substance is found almost exclusively in the fraction containing the β globulins. Experiments are now in progress with a view to obtaining the substance in a pure form.

Specific Antisera. Mr. G. F. B. Weitz has been continuing his experiments relating to the study of precipitating antisera against the blood of man and animals with the object of identifying blood meals of blood-sucking insects. Using the sera he has prepared he has been identifying the blood meals of mosquitoes which have been received from abroad dried on blotting paper. Further work has been carried out on the best means of obtaining sera with a high degree of specificity.

Staphylococcal coagulase. Dr. E. S. Duthie and Miss L. Lorenz have been engaged in the production and investigation of the properties of staphylococcal coagulase. Conditions under which variations in the yield of coagulase occur have been investigated, and it has been found that good yields are obtained when the culture is grown in the casamino acid medium described by Rogers.

The filterability, heat stability and resistance to varying hydrogen-ion concentrations of coagulase have been established.

Coagulase anti-bodies can be evoked in rabbits by injections of coagulase, which can be concentrated by suitable methods, but the results are very variable.

BIOCHEMICAL STUDIES.

The Blood Group Substances. Dr. W. T. J. Morgan and Mr. D. Aminoff have studied the action of the periodate ion on an essentially homogeneous preparation of the human blood group A-substance. There is a rapid loss of the serological activities and examination of the oxidised material shows that of the component molecules potentially susceptible to oxidation only fucose, galactose and part of the chondrosamine are oxidised. Formaldehyde and formic acid but not acetaldehyde or ammonia are produced during oxidation. The amount of the former substances produced can be used to estimate the chain length of the polysaccharide unit. These substances are produced in approximately equimolecular quantities and agree with a molecular weight of 1800 for the unit. Mild acid hydrolysis of the A-substance readily eliminates the fucose and other evidence suggests that this sugar is a non-reducing end-group with a pyranose ring structure. The two naturally occurring hexosamines, glucosamine and chondrosamine, have been identified as components of the A-substance and their discovery represents the first recognition of the two amino-sugars occurring together in one substance.

In collaboration with Dr. R. Grubb (Sweden), Dr. Morgan has examined the reactivity of human erythrocytes and secretions with an anti-serum specific for a new human blood group character known as "Lewis" and it has been observed that the so-called "Lewis positive" character of a blood is intimately correlated with the secretor-nonsecretor status within the ABO classification, "Lewis positive" adult persons being nonsecretors. These studies have also revealed the presence of an additional soluble mucoid material the serological properties of which indicate that it is a product of a gene allelomorphic with the "Lewis" gene. Dr. Morgan and Mr. E. F. Annison have elaborated methods for the isolation of mucoid materials associated with these new blood group characters and it has been found that in many respects the specific substances are similar to the group A-substance. Their frequent occurrence in a water-soluble form in human tissue fluids and secretions has been largely responsible for the rapid progress that has been made towards their isolation and identification.

Dr. J. F. McCrea is studying the power of the various blood group mucoids, and similar materials obtained from human erythrocytes, to inhibit the agglutinating action of heated Lee influenza virus. It is hoped as a result of these investigations to determine the nature of the component of the red-cell surface which is responsible for the fixation of virus.

Toxins and Enzymes. Dr. M. G. Macfarlane has continued studies on the hæmolysis of erythrocytes from different species of animals by *Cl. welchii* and *Cl. hæmolyticum* toxins. These toxins are known to be "hot-cold" lysins, so that the primary enzymic effect of the hæmolysin must be differentiated from the secondary lysis which occurs if the physical conditions of the system are changed, e.g., by cooling or dilution. The enzymic effect has now been correlated with the decomposition of the phospho-lipin of the cells, indicating that the primary action is that of the lecithinases of the toxins, which potentiate the secondary lysis. The effect of variation in the concentrations of enzyme and cells is being studied.

Dr. Macfarlane has also examined, in collaboration with Dr. E. W. Hurst (Imperial Chemical Industries), the enzymic activity of concentrated suspensions of different kinds of virus, obtained from infected allantoic fluid. Although results which were positive by comparison with normal fluid were obtained, they are inconclusive as it was not possible to rule out the presence of enzymes liberated from the host cells by the action of the virus.

Bacterial Antigens. Mr. K. A. Smith and Dr. Morgan have continued their efforts to obtain an homogeneous preparation of the O somatic antigen of *Shigella shigæ*. The material ultimately obtained was free from nucleic acid and lipoid and it seems that neither of these

materials is essential for the manifestation of antigenicity. The simplest antigenically active material so far obtained consists of a complex of polysaccharide and a protein moiety. A more detailed examination of the physical chemical and immunological properties of the material is being undertaken.

Dr. J. D. Feinberg and Dr. Morgan have examined further the main serologically specific components of two different group specific forms of *Trichomonas fœtus*. Non-antigenic carbohydrate materials which possess strong *Trichomonas fœtus* specificity have been obtained and their general properties recorded. These materials have been used by Dr. M. Robertson for skin-tests in experimental animals.

Gramicidin. Dr. A. T. James has investigated the nature of the linkages in gramicidin D most susceptible to acid hydrolysis and has isolated from the partial hydrolysis products short chain peptides containing ethanolamine, glycine, alanine and valine. The methylation of gramicidin to give the methyl ester reveals the presence of two hydroxyl groups in the molecule. Examination by means of two dimensional chromatograms and counter-current distribution of the acid hydrolysis of the methylated gramicidin shows the presence of six residues in normal gramicidin and ten in the products obtained from gramicidin D. Attempts are now being made to identify the break-down products of this latter material.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Examination of Sera. At the request of the Medical Research Council's Pneumokoniosis Research Unit, Dr. R. A. Kekwick has examined electrophoretically a group of sera from cases of pneumokoniosis. The experiments were in the nature of a control, but some of the sera showed substantial increases in the proportion of gamma globulin.

An investigation was carried out on normal human plasma which had been irradiated with ultra-violet light, with a view to the inactivation of the factor giving rise to post transfusion jaundice. Control and irradiated plasma, supplied by the Connaught Laboratories, Toronto, Canada, were found to be indistinguishable on electrophoretic and ultracentrifugal examination. Dr. E. F. McCarthy was able to find no deviation in osmotic behaviour between the control and irradiated samples.

Dr. Kekwick and Dr. McCarthy showed that bovine plasma despeciated by a treatment involving heating with formaldehyde was grossly altered in its electrophoretic and ultracentrifugal behaviour, and exhibited only 10% of the normal osmotic pressure.

Dr. Nicholas Martin (St. George's Hospital), has continued to use the facilities of the laboratory for the examination of pathological sera, particularly in relation to liver failure.

Dr. McCarthy and Dr. Kekwick were able to show that the fluid of the rabbit blastocyst, seven to eight days after fertilisation had occurred, was very similar in electrophoretic and ultracentrifugal behaviour to normal rabbit plasma. The investigation was made at the request of Professor Rogers Brambell (University College of N. Wales), who supplied the material, and the implications of the findings are discussed in a paper by him.

Dr. McCarthy and Dr. E. I. McDougall (Rowett Research Institute, Aberdeen), have investigated the effect of delayed colostrum feeding on lamb serum proteins, the immune globulin content of colostrum and the presence of protein in the lamb's urine. Lambs from ewes immunised during the latter part of pregnancy with *B. typhosus* H antigen were either allowed to suck at birth or were bottle-fed for varying periods and then fostered on to recently lambed ewes. Colostrum showed a rapid decrease in immune globulin during the first 2 - 3 days after lambing. Sera of sucking lambs showed a sudden increase in globulin, mainly γ globulin and in agglutinin. Immune globulin could be absorbed up to 29 hours after birth. After 48 hours, however, this is no longer possible. The urine of sucking lambs also showed a marked proteinuria during the first day or two after birth. The protein present included globulin and had an appreciable agglutinin titre.

Blood Clotting Studies. Mr. J. W. Lyttleton has continued the study of blood clotting factors. Investigations have been carried out on the nature of antithrombin occurring in normal human plasma. Electrophoretic separation of plasma components, together with fractional precipitation by various agents, indicates that the activity is associated with the alpha-globulin fraction. The role of heparin as an antithrombic agent is also being studied, and a possible connection between the antithrombic and proteolytic systems of plasma is being investigated.

Ultrasonic Vibrations and the Protein Molecule. Dr. C. J. B. Bradish continued his work on the effects of ultrasonic vibrations. Ultrasonic irradiation at frequencies of 500-1000 KC/S at 1-6 watts/ml. solution, in the presence of an air interface, produces no significant change in the sedimentation behaviour of egg albumin, human serum proteins and human carboxyhæmoglobin. The electrophoretic behaviour of human serum proteins is similarly unaffected. A slight coagulation of all proteins occurs during irradiation, without the properties of the protein remaining in solution being altered.

Experiments with Helix pomatia hæmocyanin and its dissociation products have failed to confirm a splitting mechanism suggested by S. Brohult, the end product found being extremely polydisperse.

Studies with viable organisms, especially *Trichomonas fœtus* indicate a much greater susceptibility to ultrasonic irradiation, attributable to the fractional forces arising when the biological unit is too large (15 μ) to follow the motion of the medium. Units smaller than 0.5 μ follow the motion of the medium completely, and any modification in properties in them occurs as a result of the numerous sequelæ of cavitation.

Human Plasma and Plasma Products. During the year the Blood Products Research Unit continued the preparation of dried human plasma and plasma fractions for clinical use. Approximately 20,000 bottles of plasma, 3,000 bottles of fibrin foam, 3,750 ampoules of thrombin and 750 ampoules of fibrinogen have been issued. In addition 2,500 ampoules of gamma globulin have been sent to the Public Health Laboratory for clinical trial in cases of measles. Plasma fractionation products may now be dried in ampoules which allow glass sealing after they are nitrogen packed, and should prevent the deterioration of the proteins by moisture. Miss N. M. E. Haysom has carried out the bacteriological tests on plasma and plasma products and the subsequent classification of contaminating organisms.

Miss M. Nance joined the Unit in November, and has been in control of the biochemical tests on the plasma fractionation.

Dr. E. A. McCulloch is investigating the incomplete type of Rh antibody, and the isolation of the blood protein necessary to activate this antibody.

Dr. Kekwick and Dr. Mackay have adapted the ether fractionation to plasma, and clinical trials of the gamma globulin so prepared indicate that the intramuscular injection of 250 mg. will suppress measles in small children.

Work is in progress on the isolation of other plasma proteins.

NUTRITIONAL STUDIES.

Normal and synthetic diet for rats. Miss A. M. Copping assisted by Miss P. J. Crowe has been studying growth of rats on normal and synthetic diets with a view to defining the adequacy of diets in use for the rat colony and for experimental work on the vitamin B complex.

An effort has been made to obtain a growth curve for the normal stock rats and to calculate the growth constant for the Lister strain of black and white rats according to Zucker's formula which permits the plotting of growth as a straight line based on the equation :

$$\log W = -\frac{k}{t} + \log A$$

where W is the weight at time t, A the weight approached asymptotically in the adult animal, log A the intercept of the straight line and k the slope of the line which characterises growth. The value for k is obtained from the equation :

$$k = \frac{\log W_2 - \log W_1}{\frac{1}{t_1} - \frac{1}{t_2}}$$

The k for the Lister stock calculated from the small sample we were able to study appears to be rather greater than that found by Zucker for normal rats. For animals on synthetic diets the values for k are irregular. No significant differences in growth have been found with different sources of casein when liver extract was given or when the vitamin supplement was entirely synthetic.

Effect of Vitamins on Gastric Conditions. Miss E. M. Hume has continued her studies of vitamin A in relation to the stomach of human beings and of rats. In the human studies she has been assisted firstly by Miss V. R. G. Pond and later by Miss Crowe and in the rat studies by Miss H. H. Smith.

In human beings, the cases of peptic ulceration or of gastric pain without ulceration, treated with vitamin A as out-patients at the Royal Free Hospital, have been further followed up. Healing of the ulcer has been demonstrated radiographically in some cases. Continuous treatment for from 6 to 10 weeks seemed the most satisfactory. Prolongation of continuous treatment for long periods caused relapse in a few cases. After an interval of from 6 to 12 months without treatment, pain might return, and another course of 6 weeks' treatment was then necessary.

The cases studied at the Medical Branch of the Post Office at Mount Pleasant in collaboration with Dr. V. C. Medvei have also been followed up. In all, a good series of about 40 patients was obtained, and the results confirmed those obtained at the Royal Free Hospital. It was planned to extend this series of observations and to maintain a control group simultaneously with a treated group. Dummy capsules were obtained for this purpose but, with the coming of the National Health Service, the clinic at Mount Pleasant was closed, and it has not been possible so far to do more than follow up the cases already treated.

In rats, the search for the factor which prevents proliferation of the gastric epithelium when the animals are deprived of vitamin A has been continued. Efforts to find the factor in casein prepared in various ways have proved unsuccessful, and recourse has been had to flour diets which were used some years ago in Cambridge, and with which proliferation did not take place when the diet was deficient in vitamin A. Flour of 85 per cent. extraction has been used, one sample bleached with agene and the other unbleached. In a preliminary experiment with 18 rats, epithelial proliferation was not quite absent but was very much less than with any of the diets tried since the original observations were made in Cambridge. The lesions which did occur did not differ greatly whether the flour was bleached or unbleached, and the rats receiving unbleached flour did not survive any longer than those receiving bleached flour.

Biosynthesis of nicotinamide by intestinal bacteria. Dr. P. Ellinger with Dr. Emmanuelowa have improved methods for the quantitative estimation of a number of intestinal bacteria contained in fæces and cæcum content of rats. By means of these methods the effect of changes of diet and of some drugs on the constitution of the intestinal flora has been investigated and related to the urinary output of nicotinamide metabolites.

Effect of tryptophan on the nicotinamide formation in rats and bacteria. To study the chemical mechanism of a potential direct conversion of tryptophan into nicotinamide Dr. Ellinger and Dr. Abdel Kader have examined the effect of various methyl substituted tryptophans on growth and nicotinamide synthesis by *Bact. coli* and mixed cultures from the rat's cæcum content. All tryptophans substituted in the indole nucleus inhibit nicotinamide synthesis in doses not affecting growth. The enzyme systems of *Bact. coli* responsible for the synthesis of nicotinamide can be purified to some extent and freed from cell debris. Nicotinamide is synthesised by this enzyme only if sources of nitrogen other than tryptophan are available. This, as well as some other results, can best be explained by a kind of catalytic effect of tryptophan on the synthesis.

Metabolism of nicotinamide and related compounds as affected by diet. Dr. Ellinger and Dr. Abdel Kader have found that on a cabbage diet, rabbits and other than omnivorous animals, deaminate nicotinamide to nicotinic acid and methylate the latter to trigonelline. When cabbage is replaced by oats no marked change occurs. When, however, the animals are fed on a meat bread diet the methylating mechanism is entirely, and the deaminating mechanism partly, suppressed, but the aminating capacity of the omnivorous species is not acquired. Return to a cabbage diet brings the metabolism back to its original condition after some weeks.

Heredity of the nicotinamide methylating mechanism in rats. Dr. Ellinger has found that in two strains of rats used by him in metabolism experiments, the daily nicotinamide methochloride output and the response to injected nicotinamide show considerable quantitative

differences. Both are low in an albino and high in a black and white strain, when the animals are kept under identical conditions of diet and housing. This is caused by differences in the methylating mechanism of the liver. By cross breeding the two strains it is found that the differences in output are caused by hereditary factors.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Bacteriological Studies. The Medical Research Council's Unit for Bacterial Chemistry, directed by Sir Paul Fildes, has continued work covering a wide field in the study of bacterial growth and metabolism.

Subjects for research during the past year have been the purification and crystallization of bacterial enzymes by Dr. D. Herbert; the "training" and mutation of typhoid bacilli to synthesise tryptophan from ammonia by Sir Paul Fildes and the use of isotypes to follow the mechanism of this synthesis by Dr. G. H. Smith; co-factors for growth of bacteriophage in coliform organisms by Mr. D. Kay, adaptive enzyme formation by Dr. M. R. Pollock and Mr. S. D. Wainwright, effects of trace metals on production of enzymes by Miss J. Pinsent, the isolation, purification and synthesis of long-chain fatty acids by Dr. G. A. Howard and their role as inhibitors or stimulators of bacterial growth by Dr. Pollock and Miss B. W. Boughton.

Dr. A. J. P. Martin has been temporarily attached to the Unit and has begun work in collaboration with Dr. Howard on a chromatographic method for the separation and purification of the higher fatty acids.

Nutritional Studies. Dr. S. S. Zilva and Dr. H. A. Painter have continued their investigation on the effect of *l*-ascorbic acid and of bacteriostatic agents on the degradation of high doses of *l*-tyrosine by guinea-pigs. They found that although in the absence of *l*-ascorbic acid from the diet or on the administration of bacteriostatic agents to the animals there was an accumulation of hydroxyphenyl compounds in the large intestine in both cases, the destruction of these compounds in the body proceeded along different routes. In the former case these substances mostly entered the blood stream and were imperfectly degraded in the system, as the *l*-ascorbic acid content of the tissues was below a certain level, the intermediate products of degradation being excreted by the kidney: in the latter case the accumulated hydroxyphenyl compounds did not enter the blood stream in large quantities but were mainly degraded during their passage along the lower reaches of the gut, the remainder being excreted in the fæces.

An investigation extending over a period of seven years has been carried out by Dr. Zilva in collaboration with Mr. M. B. Crane (Sir John Innes Horticultural Institution), on the influence of environment and genetic constitution on the formation of *l*-ascorbic acid in tomatoes. The main conclusions were that light, probably of short wave-lengths, was chiefly associated with the formation of *l*-ascorbic acid in the tomato plant and that the appearance of lycopin on ripening did not play any part in this formation. Diploid tomatoes were found to be more influenced by light in this respect than were tetraploid fruits. The reproducibility of various observations made by previous workers has been established.

Zacho's claim that the existence of "vitamin P" could be demonstrated by the application of negative pressure to the lumbar region of guinea-pigs on a scorbutic diet could not be confirmed by Dr. Zilva.

Blood Group Studies. The work of this Unit under the direction of Dr. R. Race has been continued.

Allelomorphs at the locus for the Rh genes D and C having been observed without much difficulty, a fairly wide net was cast for allelomorphs at the E locus, but so far without success. Fortune, however, rewarded the work with some unexpected observations on the quantitative gene antigen relationships: the gene E, for example, is influenced in the quantitative aspect of its expression by the fellow genes D, C, etc., in its genotype.

Many absorptions and elutions of the mixed Rh anti-sera such as anti-D + C and anti-D + E have been carried out in the hope of seeing somewhat more clearly the nature of these antibodies.

The complete blood groups have been determined of many normal families, and of families carrying disease genes. These family studies have helped to consolidate the position of the

"new" blood group systems—Lutheran, Kell and Lewis, and the recent most important subdivision of the MN system.

The long-term search for genetic linkage between blood group genes and disease genes continues.

The observation of Andresen that the "Lewis positive" blood group, in adults, depends, unlike all other known blood groups, on a recessive gene, has been confirmed and also the work of Grubb and Morgan which demonstrated the very close association between the presence of the Lewis antigen on the red cells and the absence of the ABH antigens in the saliva.

The unit works in close collaboration with the Ministry of Health Blood Group Reference Laboratory under Dr. A. E. Mourant.

Owing to the generosity of Dr. L. K. Diamond, Miss Sanger was enabled to investigate in Boston a very fine collection of antisera set aside for her at the Blood Grouping Laboratory, The Children's Hospital.

The National Collection of Type Cultures. The collection of yeasts was transferred to the Institute of Brewing and the reorganisation of the Collection, started in 1946, has been continued. Certain groups of organisms (Brucella, Micrococcus, Proteus and Staphylococcus) have been checked in detail and atypical strains discarded. About 450 new strains have been added to the Collection, and some 6,000 cultures distributed during the year.

Dr. Cowan and Miss Shaw have started a comparative study of the cultural characters of micrococci, staphylococci, and sarcinas in an attempt to classify these organisms more satisfactorily.

The Collection is now part of the Commonwealth Collections of Micro-organisms, set up on the recommendation of the Commonwealth Scientific Conference of 1946, and acts as a bureau for information on cultures of bacteria maintained in different laboratories in this country.

MINISTRY OF HEALTH.

Blood Group Reference Laboratory. Under the direction of Dr. A. E. Mourant the laboratory has continued to select, prepare and supply blood grouping sera of all kinds in increasing amounts to the National Transfusion Service, the country generally, and numerous users abroad.

Over seven hundred sera from cases of suspected immunization by pregnancy and by transfusion have been examined. Among them a number of very rare and valuable blood grouping sera have been recognised and made available for research.

Over one thousand specimens of blood from Africa, Iceland, India, Siam and other places abroad have undergone detailed blood group testing as a contribution to the ethnological investigation of the populations concerned.

The laboratory has helped English, Commonwealth and foreign laboratories to start blood grouping work, by giving personal instruction, by supplying testing serum, and by blood grouping the laboratory staffs.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the Director and all his co-workers of the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

H. H. DALE.

Chairman of the Governing Body.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1949.

FINANCIAL REPORT OF THE GOVERNING BODY.

1. The Balance Sheet for the year ended 31st December 1949 shows balances to the credit of the various funds as follows: Capital Fund £697,199; Specific Funds £114,912; Contingency Reserve £73,807 and Bequest Funds £17,775.

2. The General Fund Income and Expenditure Account shows the income for the year as £87,961 compared with £106,114 in 1948. Expenditure amounted to £84,932 against £82,366 last year. The surplus for the year is £3,029 as compared with £23,748 in 1948. The fall in Sales accounts for most of the difference.

3. The year's surplus of £3,029 shown by the General Fund Income and Expenditure account has been transferred to the Contingency Reserve.

4. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £6,309, £5,199 and £1,976 respectively.

5. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

PAUL FILDES, *Acting Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

11th May, 1950.

BALANCE SHEET

(1948) £		£	£
	Capital Fund :—		
	Donations, &c., received to date from the following :—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Berridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers' (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)	500	
21,097	Other Donations and Legacies (1891-1938)	21,097	
	General Fund Income and Expenditure Account Accumulated		
337,804	Surpluses as at 31st December, 1948	337,804	
697,199			697,199
	Specific Funds :—		
75,015	Sinking Fund for Freehold Buildings	77,931	
36,696	Pension Fund	36,981	
111,711			114,912
	Contingency Reserve :—		
	As at 31st December 1948	70,778	
	Add Surplus on General Fund Income and Expenditure Account, 1949	3,029	
70,778			73,807
879,688			885,918
	Current Liabilities :—		
12,224	Creditors and accrued charges	11,931	
672	Balance of Cancer Research Legacy (1937)	672	
12,896			12,603
892,584			898,521
	Bequest Funds :—		
9,476	Jenner Memorial Studentship Fund	9,342	
7,726	Morna Macleod Scholarship Fund	7,935	
498	Bacot Bequest Fund	498	
17,700			17,775
£910,284			£916,296

PAUL FILDES, *Acting Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have obtained all the information and explanations which to the best of our knowledge and belief were
far as appears from our examination of those books. We have examined the above Balance Sheet and annexed
amount of £8,150 due from a foreign Government which has not been agreed and which may be partly irrecover-
given to us the said accounts amplified by the information given in paragraph 4 of the Financial Report of the Gov-
Sheet gives a true and fair view of the state of the Institute's affairs as at 31st December, 1949, and the General

London, 11th May, 1950.

31st DECEMBER. 1949.

(1948) £		£	£	£
	Fixed Assets:—			
	FREEHOLD PROPERTY at cost:			
73,717	Land and Buildings, Chelsea	73,717		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,222	
	(*Note*: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	LEASEHOLD PROPERTY:—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,448		
286			221	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
	(*Note*: *Additions and replacements since 31st December,*			
98,980	*1920 have been charged to Revenue*)		—	98,915
	Quoted Investments and Uninvested Cash relating to General and Specific Funds:—			
		Quoted Investments at cost less amounts written off	Uninvested Cash	
608,562	General Fund	630,719		630,719
75,015	Sinking Fund for Freehold Buildings ..	77,801	130	77,931
36,696	Pension Fund	35,543	1,438	36,981
720,273		744,063	1,568	745,631
				745,631
	(*Market Value of Investments on London Stock Exchange £763,174*)			
	Current Assets:—			
32,809	Debtors and Payments in advance			33,135
40,522	Cash at Bankers and in hand			20,840
73,331				53,975
892,584				898,521
	(*Note*: *See paragraph 4 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts*).			
	Quoted Investments and Uninvested Cash relating to Bequest Funds:—			
		Quoted Investments at cost	Uninvested Cash	
9,476	Jenner Memorial Studentship Fund	8,545	797	9,342
7,726	Morna Macleod Scholarship Fund	7,606	329	7,935
498	Bacot Bequest Fund	—	498	498
17,700		16,151	1,624	17,775
				17,775
	(*Market Value of Investments on London Stock Exchange £14,289*)			
£910,284				£916,296

TO THE MEMBERS.

necessary for the purposes of our audit. In our opinion proper books of account have been kept by the Institute so Income and Expenditure Accounts which are in agreement with the books of account. Debtors include an able. Subject to this remark in our opinion and to the best of our information and according to the explanations erning Body give the information required by the Companies Act, 1948, in the manner so required and the Balance Fund Income and Expenditure Account gives a true and fair view of the surplus for the year ended on that date.

COOPER BROTHERS & CO.,
Chartered Accountants. } *Auditors.*

INCOME AND EXPENDITURE ACCOUNTS

General

(1948)		
£		£
40,241	Salaries and Wages	39,318
—	Emoluments of a member of the Governing Body in a Managerial capacity	2,148
1,535	Premiums on Federated Superannuation Policies	1,359
1,959	Rent, Rates and Insurance	2,205
4,341	Gas, Water, Fuel and Electricity	4,890
905	Office Expenses, Stationery and Printing	1,315
136	Auditors' Fee	157
340	Travelling Expenses	360
1,740	Biochemical Expenses	1,144
541	Bacteriological and Experimental Pathology Expenses	458
399	Nutrition Expenses	299
597	Biophysics Expenses	370
11,657	Serum, Vaccine and Vaccine Lymph Expenses	8,484
3,951	Animals	5,939
4,569	Animal House Expenses and Forage	4,525
4,792	Buildings, Alterations, Repairs and Renewals	6,727
685	General Apparatus and New Installations	1,376
623	Library Expenses	470
446	General Stores	342
—	Staff Canteen Loss	70
65	Amount written off Leasehold Property	65
2,844	Amount transferred to Sinking Fund for Freehold Buildings (including £2,492 Interest on Investments)	2,916
23,748	*Surplus* transferred to Contingency Reserve after charging £5,202 for additions to property and equipment included in the above expenses	3,029
£106,114		£87,961

Pension

£		£
1,210	Pensions	1,321
396	Balance added to Fund	285
£1,606		£1,606

Jenner Memorial

£		£
250	Stipend of Student	424
754	Deficit on conversion of Investment (1948)	—
£1,004		£424

Morna Macleod

£		£
215	Balance added to Fund	209
£215		£209

for the year ended 31st December, 1949.

Fund.

(1948) £		£	£
	Interest on Investments (gross):		
21,362	General Fund	21,013	
2,420	Sinking Fund	2,492	
			23,505
75,527	Sales of Sera, Vaccines, Vaccine Lymph, &c.		55,976
6,805	Rent		8,480
£106.114			£87,961

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
£1,606		£1,606

Studentship Fund.

£		£
300	Interest on Investments (gross)	290
704	Balance Deducted from Fund...	134
£1,004		£424

Scholarship Fund.

£		£
215	Interest on Investments (gross)	209
£215		£209

INVESTMENTS AT 31st DECEMBER, 1949.

GENERAL FUND.

Nominal Value		Balance Sheet Value		Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	..	£81,200
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	..	40,984
£52,000	4 per cent. Funding Stock, 1960-90	45,662	..	55,640
£64,000	3½ per cent. War Stock, 1952, or after	63,408	..	59,200
£25,000	2½ per cent. National War Bonds, 1949/51	24,750	..	25,344
£20,000	,, ,, ,, ,, 1951/53	20,000	..	20,325
£31,000	,, ,, ,, ,, 1952/54	31,000	..	31,426
£45,000	,, ,, ,, ,, 1954/56	46,595	..	45,675
£35,000	3 per cent. Savings Bonds 1955/65	35,000	..	34,825
£78,000	,, ,, ,, 1960/70	78,122	..	75,660
£10,000	,, ,, ,, 1965/75	10,000	..	9,500
£55,495	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	55,495	..	49,946
£20,000	,, ,, ,, ,, ,, 1967/72 ..	20,259	..	18,400
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	4,009
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	1,898	..	1,880
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75 ..	2,687	..	2,865
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65 ..	21,989	..	24,875
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	21,011
£2,900	Commonwealth of Australia 3½ per cent. Stock, 1950/52 ..	2,724	..	2,958
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74 ..	12,121	..	11,220
£25,000	,, ,, ,, 3 per cent. Registered Stock, 1965/67	19,800	..	24,250
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	..	908
		£630,719		£642,101

SINKING FUND FOR FREEHOLD BUILDINGS.

£10,200	4 per cent. Funding Stock, 1960-90	9,079	..	10,914
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	..	19,270
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	..	3,482
£3,700	,, ,, ,, 1960/70	3,709	..	3,589
£31,600	,, ,, ,, 1965/75	31,600	..	30,020
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	..	2,030
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	..	2,208
£26,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	6,260	..	6,016
		£77,801		£77,529

PENSION FUND.

£22,000	4 per cent. Funding Stock, 1960-90	17,165	..	23,540
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173	..	16,920
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	..	2,134
£1,000	3 ,, ,, ,, 1965/75	1,000	..	950
		£35,543		£43,544

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705	..	2,996
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986	..	1,787
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757	..	2,133
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097	..	1,040
		£8,545		£7,956

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, 3rd Issue	1,000	..	1,000
£500	3 per cent. Savings Bonds, 1960/70	500	..	485
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	..	4,002
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903	..	846
		£7,606		£6,333

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,
1950.

Chelsea Bridge Road,
London, S.W. 1.

June 21st. 1950.

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J. W. Lyttleton, M.Sc. (*Beit Memorial Research Fellow*).
B. Cinader, B.Sc., Ph.D., (*Beit Memorial Research Fellow*).

BLOOD PRODUCTS RESEARCH UNIT.

Margaret E. Mackay, M.Sc., Ph.D. (*Medical Research Council External Scientific Staff*).
Margaret Nance, B.Sc (*Medical Research Council External Scientific Staff*).
L. Vallet, B.A.
H. R. F. Arnstein, B.Sc.
Shirley A. Kent, B.Sc.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE).

W. d'A. Maycock, M.B.E., M.D., (*Superintendent of Elstree Laboratories and Estate*).
G. F. B. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc. (*Research Student*).

PREPARATION AND STUDY OF VACCINE LYMPH (ELSTREE).

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.B., B.S.

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†*Appointed Teacher of the University of London.*
**Recognised Teacher of the University of London.*
§*Working at Elstree.*

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE).

A. F. B. Standfast, M.A., Dip.Bact.
Margaret P. D. Pile, B.Sc.
F. L. Massri, Dip.Bact.
(*Egyptian Government Student*).

Margaret E. Rowatt, B.Sc.
(*Public Health Laboratory Service*).

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Blood Group Research Unit.

R. R. Race, Ph.D., M.R.C.S., L.R.C.P.
Ruth Sanger, Ph.D., B.Sc.
Helene A. Holt, B.A.
Joan S. Thompson, B.Sc.

Blood Group Reference Laboratory.

A. E. Mourant, D.Phil., D.M.
Anna M. Grove-White, M.B.
Elizabeth W. Ikin, B.Sc.
Jean Walby, B.Sc.

ADMINISTRATION.

Secretary	A. N. Drury, C.B.E., M.A., M.D., F.R.S.
Elstree Secretary and Estate Manager	F. K. Fox.
Assistant Secretary and Accountant	S. A. White, A.A.C.C.A.

Solicitor:

Field, Roscoe & Co.,
52, Bedford Square, W.C. 1.

Auditors:

Cooper Brothers & Co.,
14, George Street, Mansion House, E.C. 4.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 21st. 1950.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report of the work of the Institute for the year 1949/50.

GOVERNING BODY.

The passing of the Special Resolution to alter the Memoradum of Association of the Institute in December last has caused the following changes in the personnel of the Governing Body. Dr. A. N. Drury, formerly one of Lord Iveagh's representatives on the Governing Body is now, as Director, *ex officio* a member and in his stead Lord Iveagh has appointed Lord Balfour of Burleigh. Dr. W. T. J. Morgan has been appointed to the Governing Body as the Scientific Staff's representative.

COUNCIL.

At last year's Annual General Meeting the three retiring members of the Council, Sir Charles Harington, Sir Paul Fildes and Sir Percival Hartley, were re-elected.

The three members of the Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Dr. J. Henderson Smith, Professor M. J. Stewart, representatives of the Members of the Institute and Professor S. P. Bedson, who represents the Royal Society.

The Governing Body records with regret the deaths of Professor J. A. Ryle, a representative of the Members on the Council since 1941, and of Professor M. Greenwood, a member of the staff from 1910 to 1919, a Member from 1931 and a representative of the Members on the Council since 1938.

MEMBERS.

The death of Professor S. L. Cummins, a member since 1918, is recorded with regret.

During the year invitations to become Members of the Institute have been accepted by Professor F. W. Rogers Brambell, Dr. H. P. Himsworth, Dr. W. d'A. Maycock, Dr. M. R. Pollock, Professor Lord Stamp, Professor A. R. Todd and Mr. A. L. White.

STAFF.

After over 50 years service Mr. A. L. White, Secretary since 1926, retired on the 31st December, 1949. At a gathering on 9th January, Sir Henry Dale, on behalf of the Governing Body and past and present staff, presented Mr. White with a clock and a cheque as a memento of his long and valuable service to the Institute.

Dr. S. S. Zilva, a member of the Medical Research Council External Scientific Staff and an honorary member of the Institute staff, retired in March. Dr. Zilva joined the Biochemical Department in 1913 as a voluntary worker and during his long association with the Institute has made numerous valuable contributions to the knowledge of the actions and properties of vitamins. Miss H. H. Smith, who first came to the Institute in 1919 and who has always been closely connected with the work of the Nutrition Department, retired in April.

Miss A. M. Copping resigned in September on taking up a post at King's College of Household and Social Science.

Dr. J. Baddiley joined the Biochemical staff in September, 1949. Dr. D. Aminoff, Dr. E. M. Thain and Miss W. M. Stanier were appointed Research Assistants, and Miss G. M. Harris and Mr. G. Rummelsburg were appointed to Research Studentships.

Both Mr. H. J. Bunce and Mr. W. Taylor, after 31 years service at Elstree, have retired on pension.

The Blood Products Unit, the Blood Group Research Unit and the Blood Group Reference Laboratory (formerly Ministry of Health) of the Medical Research Council are still accommodated at the Institute.

The Bacterial Chemistry Unit has now transferred to the National Institute at Mill Hill and the National Collection of Type Cultures, housed at the Institute since 1920, to the Central Public Health Laboratory at Colindale.

The Governing Body, before surveying the scientific work carried out during the year, once again desires to record its appreciation of the continued co-operation and collaboration of the Medical Research Council with the Institute.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus pertussis. Mr. A. F. B. Standfast has continued his investigations into the antigens of *H. pertussis,* in particular those involved in protection. Experiments carried out indicate that the mouse protective antigen is distinct from the other known antigens, such as the Phase I agglutinogen and the hæmagglutinin of Keogh and North. Attempts will now be made to separate these antigens by chemical or physical means as preliminary experiments have indicated a method by which this may be achieved.

Dr. F. Massri has started an investigation into the hæmagglutinins of *H. pertussis.* As their potency can be demonstrated by a simple *in vitro* test, they lend themselves particularly well to an investigation into the part played in infection and immunity of a single antigen. A method has been evolved of extracting the antigen in an active form from bacterial cells and attempts are now being made to purify the extract further.

Miss E. Rowatt is investigating the nutrition of *H. pertussis* with a view to (a) improving the medium used for the primary isolation of the organism, and (b) the development of a medium for the production of *H. pertussis* in bulk with the optimum antigenic content. Special attention is being paid to the utilisation of amino acids during growth and an attempt is being made to discover the source of energy for the growth of the organism.

Vibrio choleræ. Miss M. P. D. Pile has continued the investigation into the part played by the mucinase and the receptor destroying enzymes of *V. choleræ* in experimental infection and immunity. Experiments are now in progress with a view to obtaining these enzymes in pure form in order that *in vivo* experiments may be carried out.

Trichomonas Studies. Work on trichomoniasis in cattle has been continued by Dr. M. Robertson in collaboration with Dr. W. R. Kerr (Department of Veterinary Research, Ministry of Agriculture, Northern Ireland).

The studies on the inhibition of the skin reaction in animals, naturally or artificially sensitised against Trichomonas antigen, have been continued and further extended by experiments with a synthetic antihistamine "phenergan." Some considerable degree of inhibition was produced but the mechanism is different from that brought about by the injection of adrenal cortical hormone or sphingomyelin.

Work on the response of very young animals to vaccination with Trichomonas antigen is being carried out with particular reference to the relation between the rise in titre and the disappearance of antibody received passively from the maternal colostrum. There seems to be a tendency for the appearance in the circulation of the new active antibody to be delayed until most of the maternal antibody has disappeared.

Miss J. Clausen has begun a study of the *in vitro* growth of *Trichomonas fœtus.*

Vaccinia Virus. In collaboration with Dr. E. Weston Hurst (Imperial Chemical Industries), Dr. D. McClean is investigating the possible relationship between "iso-allergic encephalitis" and post exanthematous encephalitis with particular reference to post vaccinial encephalitis. Groups of guinea-pigs have been sensitised in various ways with emulsions of both heterologous and homologous cerebral white matter with and without adjuvants. A few of these animals have developed paralytic symptoms and the histology of their central nervous systems is being examined. After a period which will exclude the occurrence of further cases of paralysis due to the sensitisation alone, these animals will be infected with vaccinia virus adapted to the guinea-pig and watched for the development of any abnormal symptoms.

In collaboration with Dr. C. H. Lack (Royal National Orthopædic Hospital) and Professor R. H. Thompson (Guy's Hospital), Dr. McClean and Dr. L. H. Collier are studying the influence of 2, 3-dimercaptopropanol (BAL) on the copper content of the tissues and on the proliferation of vaccinia virus. The presence of 0.05 per cent. copper in highly purified preparations of vaccinia elementary body suspensions has been reported and, since this copper can only be derived from the host's tissues, it is of interest to determine whether deprivation of copper will interfere with the proliferation of the virus. Preliminary experiments indicated that the intramuscular injection into rabbits of the maximum tolerated dose of BAL over a period of ten days significantly increases the urinary excretion and serum content of copper and reduces the amount of that element in the viscera. Intramuscular and intravenous injections of BAL over this period do not, however, significantly affect the development of lesions of vaccinia. Local inunction with BAL ointment, on the other hand, does diminish the vaccinial reaction as compared with lesions similarly treated with capsicum ointment and plain lanoline; inunction with BAL causes a paradoxical local increase in the concentration of copper in the skin which is presumably bound and is not available to the virus. The histology of these vaccinial lesions is being studied. The *in vitro* treatment of vaccinia virus with BAL significantly reduces the copper content of the virus but does not diminish its infectivity when it is subsequently inoculated on a normal animal or in the embryonated egg.

Dr. Collier is continuing his investigations into the factors influencing the survival of vaccinia virus under different conditions of storage. This work is being conducted mostly with purified elementary body suspensions, although crude vaccine pulp, glycerinated lymph, lanolinated lymph and material cultured on the chorio-allantois are also being studied. The main factors under survey are temperature, type of suspending medium, pH, the influence of drying from the frozen state, and the atmosphere in which dried preparations are stored.

Results obtained so far indicate that there is little difference between liquid and dried material as regards maintenance of infectivity when held at 0°-4°C., but suspensions dried in association with certain protein solutions hold their titre better at 22°C. and 37°C. than do the comparable liquid preparations.

Dr. Collier is also proceeding with his study of the behaviour of a dermal-adapted strain of vaccinia in the rabbit and in the embryonated egg.

Streptococcal Capsulation and Virulence. In collaboration with Dr. McClean, Mr. G. Rummelsburg is studying the cultural requirements of capsule producing streptococci with special reference to their capacity to secrete hyaluronic acid and its relation to their virulence. This work will also involve an investigation of the relationship between the factors necessary for the production of hyaluronic acid by some streptococci and hyaluronidase by others and the relative parts played by capsules in determining virulence on the one hand and by hyaluronidase in promoting local invasiveness on the other.

Bacterial Cytology. Dr. E. Klieneberger-Nobel has carried out filtration analyses by Elford's method of the L-form of *Streptobacillus moniliformis* and has shown that this growth form is filterable through gradocol membranes which retain the bacillary A-form completely.

From these experiments it was concluded that the size of the filterable particles of the L-form of *Streptobacillus moniliformis* ranges from 175 to 250 m.μ. Therefore it would appear that the size of the small elements ranges with that of the larger viruses while the bacillary A-form ranges with that of *Bact. prodigiosum*.

Dr. Klieneberger-Nobel is now engaged on a study of the life cycle of various bacteria by means of the phase microscope.

Dr. R. G. Wittler has been investigating the environmental conditions under which Phase I and Phase IV strains of *Hæmophilus pertussis* produce structures morphologically similar to the "L" forms described by Klieneberger-Nobel. It has been found that the addition of small amounts of peptone, glycine, or other amino acids to Bordet-Gengou medium enhances the production of the "L" form.

Work is now in progress on the significance of the "L" form *in vivo* and on the serological relationship between the "L" form and the bacillary form of *H. pertussis*.

Plasma substitutes. Dr. W. d'A. Maycock and Miss L. Lorenz have been engaged in preparatory experiments for the investigation of the fate of dextran in the body after injection. Several methods of extracting dextran from the various tissues have been examined and an accurate method of determining dextran in rabbit urine has been worked out. Pilot experiments on the effect of controlled acetone fractionation and hydrolysis on the molecular size of dextran in relation to renal excretion have been performed in conjunction with Dr. Colin Ricketts (Medical Research Council, Burns Unit) and, in collaboration with Dr. R. Drury (University College Hospital), similar experiments on the effect of dextran of different molecular sizes on the histological structure of various tissues are in progress. Data on the passage of dextran into the cerebro-spinal fluid are being collected.

Dextran, which is to be used in the extended clinical trial under the ægis of the Ministry of Health and Medical Research Council has been tested.

Specific Antisera. The work on the preparation of specific antisera for the identification of blood meals of hæmatophagous diptera was continued by Mr. G. F. B. Weitz. A special journey to East Africa was made in order to carry out investigations of the most suitable methods for the collection of large volumes of animal sera from African wild mammals. These sera are for use as antigens and they were preserved by freeze-drying when received in this country. This work is to be continued until a fully representative collection of the African mammalian fauna has been obtained.

A very large number of tests were made on the stomach contents of *A. aquasalis* from Trinidad in co-operation with Dr. Senior White, the malariologist. The feeding habits of this species of mosquito were studied by the precipitin reaction from catches made under normal field conditions and were compared with the results obtained when experimental baits were used. The host preferences of *A. aquasalis* studied in this way showed little resemblance to their normal habits in the field except in regard to the anthropophilic index which remained constant. The presence of cattle around habitations seemed to provide an effective means of protection to humans against mosquito bites by this species. Less than 2% of the feeds tested gave no reaction with the antisera used for identification and it is assumed that these feeds may have been made on a variety of animals, e.g., birds, rodents or bats, for which antisera were not available.

A number of tsetse fly feeds originating from the forest in Zanzibar were examined and the results showed that the most important source of food of *Gl. austeni* in that country was the bush-pig.

In connection with the precipitating antisera work is now in progress for the investigation of the nature of non-specific precipitins which appear in the serum of rabbits after repeated immunisation.

BIOCHEMICAL STUDIES.

The Blood Group Substances. Dr. D. Aminoff and Dr. W. T. J. Morgan have completed their studies on the oxidising action of the periodate ion on the human blood group A-substance and have applied the technique of quantitative paper chromatography to the acid hydrolysis products of the material before and after periodate oxidation at different pH values. The results indicate that at pH 5 only the chondrosamine end-group is oxidised, whereas at pH 7.5 the neighbouring glucosamine and to a certain extent some additional chondrosamine is also involved. Dr. Aminoff has investigated with some success additional methods for the separation of individual mucoids from the mixtures of these substances which occur naturally in cyst fluids. Progress in

this field becomes increasingly important as the number of blood group substances detectable serologically in the native tissue fluids and secretions increases.

Dr. A. T. James (Beit Research Fellow) and Dr. Morgan have developed a quantitative chromotographic technique for the separation of the two naturally occurring amino sugars, glucosamine and chondrosamine, which have been shown to be components of the different blood group mucoids. The amino sugars, after liberation from the group substance by acid hydrolysis, are converted to the 2 :4 dinitrophenyl derivatives by the action of 1 :fluoro 2 :4 dinitrobenzene. The bright yellow derivatives are then separated from the corresponding derivatives of the amino acid components of the group substance and from each other by passing through a column of kieselguhr buffered with the aqueous phase from the solvent system potassium borate (pH 9.8)/30% amyl alcohol-chloroform. The chondrosamine molecule by virtue of a pair of *Cis* hydroxyl groups forms a complex with the metaborate ion which, by increasing the solubility of the complex in the aqueous phase, retards its movement down the column and allows a separation from the glucosamine derivative to be achieved.

Dr. J. F. McCrea and Dr. Morgan are examining the materials extractable from the human erythrocyte surface in order to elaborate a technique which will allow the isolation and separation from each other of the receptors responsible for the fixation of virus and the components which carry the human blood group characters. The problem has so far proved to be a difficult one and only limited progress has been achieved.

Mr. E. F. Annison and Dr. Morgan have continued their attempts to isolate the so-called O substance which occurs in the tissue fluids and secretions of all secretors within the ABO blood group classification. The techniques developed earlier for the preparation of the group A-substance have been employed and have allowed an apparently homogeneous preparation of this material to be obtained. Physical and chemical examination of the so-called O substance indicates that it is closely similar in composition and structure to the A-substance and that it is a polysaccharide-amino acid complex.

Dr. Morgan and Mr. Annison have obtained in an essentially homogeneous condition the gene product responsible for the recently discovered human blood group "Lewis" character. It was reported last year that "Lewis" positive adult persons are "nonsecretors" within the ABO classification and the discovery that "Lewis" positive persons secrete a specific water soluble gene product shows that there are in fact no "nonsecretors" but that all persons secrete one or more of their blood group factors in a water soluble form. The results of these studies on the "Lewis" system and its relationship to the secretor-nonsecretor phenomenon within the ABO classification have allowed Dr. R. Grubb and Dr. Morgan to suggest that the "Lewis" genes and the genes of secretion most probably belong to one genetical system. It is of considerable interest to find that on the basis of its physical and chemical properties the "Lewis" factor (Le^a-substance) is very similar to the group A-substance and the so-called O factor. In view of the importance to our understanding of the mechanism of gene action, the determination of the precise differences in these closely related gene products is an undertaking worthy of serious study. The knowledge gained will be suitable for examination in the light of the available genetical data and it is hoped that a useful contribution to the biochemical aspects of human genetics will result.

Toxins and Enzymes. Dr. M. G. Macfarlane has continued a study of the variation in the hæmolytic capacity of the immunologically-distinct lecithinases present in Clostridial toxins towards erythrocytes from different species of animals. It has been found that amounts, for instance, of *Clostridium welchii* and *Cl. œdematiens* β-lecithinase which are equal when judged by their activity towards an aqueous emulsion of lecithin, hydrolyse the phospholipin of intact sheep or horse erythrocytes at very different rates, a fact which accounts for the differences in the hæmolytic action. This variation in the rate of attack upon a substrate held in a cell by enzymes which are biochemically similar, but immunologically distinct, would appear to be a basic factor in determining the virulence of a particular parasite for a particular host.

Dr. Macfarlane and Miss G. M. Harris have begun an investigation of the mode of action of *Cl. œdematiens* toxin. Miss W. M. Stanier has been studying the production of *Cl. œdematiens* toxin as a preliminary to the separation of the various components.

Bacterial Antigens. Dr. Mosimann and Dr. Morgan have continued their work on O somatic antigen isolated from cultures of *Shigella shigæ* obtained by freeze-drying the living organisms. The chemical properties of the extracted antigen gave no evidence that the earlier preparations of this material, which had been derived from cultures killed with acetone, had undergone any change due to this treatment. An examination by differential centrifugation of the antigenic complex and its component polysaccharide and conjugated protein residues is being undertaken.

Mr. D. A. L. Davies has started to investigate the autolytic enzyme system within cultures of *Shigella shigæ* and is attempting to obtain an enzyme preparation that will decompose the whole O antigenic complex into its component residues and thus avoid the use of acid as described in the earlier experiments. Mr. Davies is also studying the formation and nature of the classical "Shiga" exotoxin.

During the year Dr. J. D. Feinberg and Dr. Morgan have isolated the dominant specific substance from *Trichomonas fœtus* and are now investigating the chemical and immunological properties of this material.

Mould and Yeast Pigments. Dr. J. Baddiley and Dr. E. M. Thain have started chemical investigations on the red pigments produced by adenine requiring mutants of *Neurospora crassa* and *Saccharomyces cerevisiæ*. These substances are only formed when the organisms are grown in the presence of limited amounts of adenine and are probably polypeptides in combination with a highly unstable coloured group.

Coenzyme A studies. Dr. Baddiley and Dr. Thain are investigating the suggestion that coenzyme A, the coenzyme concerned with acetylation processes in the living cell, is a phosphorylated derivative of pantothenic acid. The synthesis of the two possible pantothenic acid phosphates is nearly complete.

Codecarboxylase. Dr. Baddiley is attempting an unambiguous synthesis of pyridoxal phosphate, the coenzyme of bacterial amino acid decarboxylation and tryptophane synthesis. One biologically inactive phosphate has been made and another isomer is in course of preparation.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Electrophoresis. In collaboration with Messrs. Hilger & Watts Ltd. (Hilger Division), Mr. J. W. Lyttleton and Dr. R. A. Kekwick have developed a new form of U tube. This "flow through" U tube is capable of semi-continuous operation for preparative electrophoresis, with optical control in the standard Schlieren optical train. The advantages it displays are simplicity of manipulation, the separation of samples without dilution and a minimum modification of standard equipment for operation.

Muscle Proteins. Dr. G. Hamoir (University of Liege) made extensive studies of the muscle proteins of the mirror carp. He was able to isolate a protein in crystalline form, similar to tropomyosin. He was also able to show with the ultracentrifuge that the state of aggregation of the myosin-actomyosin fraction was considerably influenced by the addition of ATP.

Immunological Studies. Dr. B. Cinader has studied chromatographically the hydrolysis products from a streptolysin S preparation, which had been purified by fractionation in methanol containing systems at low temperature. Nucleic acid, ribose and several amino acids were identified as constituents of streptolysin S.

In collaboration with Mr. Weitz the beta and gamma globulin antitoxins from horse tetanus anti-toxin are being studied. Following a preliminary salt fractionation of the anti-toxic serum, electrophoretically pure samples of beta and gamma globulin have been prepared with the flow through U tube, and their life and ability to pass the capillary membrane *in vivo* are being examined.

Preliminary studies have been initiated on enzyme antibodies.

Blood Clotting Studies. Mr. Lyttleton has continued his studies of the anti-thrombic activity of normal human plasma and the effect of heparin on this property.

A quantitative measure of anti-thrombic activity has been established and the kinetics of the reaction studied. The role of heparin has been shown to comprise an immediate anti-thrombic action consequent upon the formation of a reversible heparin-thrombin complex, and a catalytic effect in conjunction with a co-factor present in plasma, causing further thrombin inactivation.

The relation between normal plasma anti-thrombin, which is associated with alpha-globulin, and the heparin co-factor is being further investigated.

Pathological Sera. Dr. N. H. Martin (St. George's Hospital) has continued his studies of sera from cases showing liver damage, with particular reference to the occurrence in such cases of molecules of abnormal size and shape.

Human Plasma and Plasma Products. The Blood Products Unit has continued to produce dried human plasma and plasma fractions for the Ministry of Health. In all, 18,500 bottles of plasma have been prepared and dried. The plasma fractions prepared and distributed amount to 900 ampoules of fibrinogen, 3,300 bottles of fibrin foam, 3,800 ampoules of thrombin, and 3,700 ampoules of gamma globulin. Batches of gamma globulin have been divided, half the batch concentrated by drying from the frozen state in bulk, reconstituted in smaller volume, bottled to give 250 mg. per ampoule and held as a liquid. The other half batch has been ampouled before drying in the ordinary way, in quantities containing 250 mg. A clinical trial will be made to establish a comparison in potency between the material held in the liquid and dried state. This trial will be carried out, as in previous years, by the Public Health Laboratory Service.

The ether fractionation system for human plasma proteins has been further developed by Dr. Kekwick and Dr. M. E. Mackay to provide purified gamma globulin for measles prophylaxis.

By a three-stage process a product which is 90-95% gamma globulin is obtained, the overall yield of gamma globulin being 80% of that present in the starting material.

A further purification provides electrophoretically pure gamma globulin in high yield.

Dr. Mackay has adapted the ether fractionation technique to isolate proteins of immunological significance from bovine serum and plasma. A fractionation with sodium sulphate has also been tried and it could be adapted to prepare electrophoretically homogeneous gamma globulin from the serum of normal and immune cows.

Miss M. Nance, who has been responsible for the routine biochemistry for the Unit, has continued the work begun by Dr. Record in attempting to isolate the antihæmophilic globulin precipitated with fibrinogen.

Miss N. M. E. Haysom has carried out all the bacteriological work for the Unit, and kept the relevant records.

Mr. L. Vallet has been engaged in developing the apparatus and technique for the sterilisation of plasma and serum by ultra-violet light.

NUTRITIONAL STUDIES.

Heredity of the Nicotinamide Methylating Mechanism in Rats. Dr. P. Ellinger has continued his experiments on the heredity of the nicotinamide methylating mechanism in rats. It can be shown by cross breeding that the height of the nicotinamide methochloride elimination is controlled by heredity. There is so far no proof that it is controlled by a single gene and the controlling factors are not associated with fur colour or with sex. The high nicotinamide methochloride elimination is probably a recessive character.

One hundred and six offspring of fourteen matings of parents with high nicotinamide methochloride elimination all showed the same high elimination. When, however, the male rats with high output were treated with nitrogen mustard the day before mating with females with high output some of the offspring showed a low nicotinamide methochloride output, although that of the treated fathers remained unaffected. In the following generations the nicotinamide methochloride elimination returned to the original level. This phenomenon cannot be explained by a point mutation, but it is conceivably produced by the effect of the nitrogen mustard on plasmogenes or modifying genes.

The Effect of Streptomycin treatment on the Intestinal Flora and the Nicotinamide Status in Man. In collaboration with Dr. E. Nassau (County Hospital, Harefield, Middlesex), an examination has been initiated by Dr. Ellinger, of the intestinal flora of tuberculous patients and the nicotinamide methochloride elimination before, during and after parenteral injection of streptomycin. No decisive results can so far be recorded, except that during streptomycin administration the intestinal flora was affected significantly in all cases, the coliform bacteria disappearing.

Metabolites of Nicotinamide. N-methyl-2-pyridone-5-carboxylic acid amide and quinolinic acid have been reported to be metabolites of nicotinamide in certain species and under certain circumstances. With a view to examining these claims Dr. Ellinger has started to develop assay methods for both compounds.

Fat Soluble Vitamins. The work on fat soluble vitamins within the Institute during the last ten years has devolved to a large extent on Miss E. M. Hume and, very appropriately, she acted as Secretary to the International Conference on Standardisation of Fat Soluble Vitamins held in London last year.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

***L*-ascorbic acid and the degradation of the phenolic group in *L*-tyrosine.** Dr. S. S. Zilva and Dr. H. A. Painter carried out an investigation on the rate of disappearance of the phenolic group of *L*-tyrosine in the presence of suspensions of liver from saturated and from scorbutic guinea pigs. The reaction proceeded at a higher rate when suspensions from livers of saturated animals were used. This was found to be due to the presence of higher concentrations of *L*-ascorbic acid *per se* and the action could be traced to the oxidation-reduction potential of the compound. The kinetics of the reaction were studied in detail. The evidence affords conclusive proof that the higher requirement of *L*-ascorbic acid needed to degrade fully high doses of *L*-tyrosine is due to a reaction which lies outside the normal metabolic processes of these animals.

The alkaline phosphatase concentration of the tissues of young guinea pigs during the development of scurvy. With Mr. H. R. Perkins Dr. Zilva has investigated the influence of scurvy and of loss of weight in young guinea pigs on the alkaline phosphatase content of their serum and the zones of provisional calcification. Whilst in loss of weight the decrease in the phosphatase in all the tissues examined was similar, in scurvy the serum phosphatase fell with the onset of the early scorbutic lesions, but the diminution in the enzyme concentration in the bone tissues only became evident several days later, when the scorbutic condition was very acute. It is assumed that the fall of the phosphatase in the zones of provisional calcification of young scorbutic guinea pigs may be due to a disturbance in the function of the osteoblasts caused by local scorbutic lesions. In scorbutic adult guinea pigs there is a fall only in the serum phosphatase. *L*-ascorbic acid is not the direct regulating agent of the phosphatase content of the tissues; the latter depends indirectly on the pharmacological action of the vitamin.

Blood group studies. The main work of the Unit under the direction of Dr. R. Race has been the testing of about 400 persons for all the known blood groups. The results established the serological independence of certain of the groups, an independence which had previously been assumed but not proved. Immunisation of about 100 of these volunteers has been started in the hope that some of them may produce new antibodies or antibodies whose existence is to be expected for theoretical reasons.

The results of the family investigations of the past few years have been assembled and the calculations which will show whether any of the blood groups are genetically linked are about to begin.

Further studies of the inheritance of the Rh, MNS and Lutheran groups have been made. The inheritance of the "new" blood group "Duffy," recently discovered by the Medical Research Council Blood Transfusion Research Unit, has been studied in 60 families.

Mr. John Hall has been working in the Unit preparatory to studying the blood groups of animals for the Agricultural Research Council.

The Unit is working in close collaboration with the Blood Group Reference Laboratory, under Dr. A. E. Mourant.

Blood Group Reference Laboratory. The Laboratory has continued its routine work of selecting, preparing and supplying blood grouping sera of all kinds to users in Great Britain and abroad. There has been a considerable increase in the number of sera examined from cases of suspected immunisation by pregnancy and transfusion. Further examples of very rare types of antibody have been detected and the sera containing them made available for use in research. Detailed serological and genetical studies have been carried out on the more important cases, with a view to publication.

Anthropological blood group studies have been carried out on persons from India, Ceylon, Egypt, Northern Sudan, Ethiopia, Kenya and Spain.

The amount of instruction in blood grouping methods given to persons from laboratories in England, the British Commonwealth and elsewhere has greatly increased. Laboratories beginning to carry out Rh testing have been helped by supplying serum and by testing the blood of members of the staffs of the laboratories. In one such case a new type of Rh antigen was found in the blood of an Italian and has formed the object of a detailed research.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

PAUL FILDES,

Acting Chairman of the Governing Body.

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR

AMINOFF, D., MORGAN, W. T. J. and WATKINS, W. M. — Studies in Immunochemistry. The isolation and properties of the human blood group A substance. *Biochemical Journal*, Vol. 46, 1950.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1950.

FINANCIAL REPORT OF THE GOVERNING BODY.

1. The Balance Sheet for the year ended 31st December 1950 shows balances to the credit of the various funds as follows: Capital Fund £697,199; Specific Funds £117,899; Contingency Reserve £88,843 and Bequest Funds £17,697.

2. The General Fund Income and Expenditure Account shows the income for the year as £129,101 compared with £87,961 in 1949. Expenditure amounted to £114,065 against £84,932 last year. The surplus for the year is £15,036 compared with £3,029 in 1949.

3. The year's surplus of £15,036 shown by the General Fund Income and Expenditure account has been transferred to the Contingency Reserve.

4. The Bacot Bequest Fund has been closed, the balance having been used to defray part of the cost of equipping the staff canteens at Chelsea and Elstree.

5. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £8,592, £4,845 and £1,862 respectively.

6. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

HENRY H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

11th May, 1951.

BALANCE SHEET

(1949) £		£	£
	Capital Fund:—		
	Donations, &c., received to date from the following:—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Berridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers' (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)	500	
21,097	Other Donations and Legacies (1891-1938)	21,097	
	General Fund Income and Expenditure Account Accumulated		
337,804	Surpluses as at 31st December, 1949	337,804	
697,199			697,199
	Specific Funds:—		
77,931	Sinking Fund for Freehold Buildings	80,966	
36,981	Pension Fund	36,933	
114,912			117,899
	Contingency Reserve:—		
	As at 31st December 1949	73,807	
	Add Surplus on General Fund Income and Expenditure Account, 1950	15,036	
73,807			88,843
885,918			903,941
	Current Liabilities:—		
11,931	Creditors and accrued charges	11,992	
672	Balance of Cancer Research Legacies (1937/50)	772	
12,603			12,764
898,521			916,705
	Bequest Funds:—		
9,342	Jenner Memorial Studentship Fund	9,420	
7,935	Morna Macleod Scholarship Fund as at 31st December, 1949 — 7,935		
	Add Balance of William A. Macleod Bequest — 225		
	Balance of Income, 1950 — 117		
		8,277	
498	Bacot Bequest Fund	—	
17,775	(*Note: See paragraph 4 Governing Body's Financial Report.*)		17,697
£916,296			£934,402

HENRY H. DALE, *Chairman of Governing Body.*

JOHN ANDERSON, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have obtained all the information and explanations which to the best of our knowledge and belief were
far as appears from our examination of those books. We have examined the above Balance Sheet and annexed
best of our information and according to the explanations given to us the said accounts amplified by the informa-
Companies Act, 1948, in the manner so required and the Balance Sheet gives a true and fair view of the state of the
and fair view of the surplus for the year ended on that date.

London, 16th May, 1951.

31st DECEMBER, 1950.

(1949) £		£	£	£
	Fixed Assets :—			
	FREEHOLD PROPERTY at cost :			
73,717	Land and Buildings, Chelsea	73,717		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,222	
	(*Note*: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	LEASEHOLD PROPERTY :—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,514		
221			155	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS :—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,915	(*Note*: *Additions and replacements since 31st December, 1920 have been charged to Revenue*)		—	98,849

Quoted Investments and Uninvested Cash relating to General and Specific Funds :—

		Quoted Investments at cost less amounts written off	Uninvested Cash		
630,719	General Fund	645,644		645,644	
77,931	Sinking Fund for Freehold Buildings ..	80,717	249	80,966	
36,981	Pension Fund	35,543	1,390	36,933	
745,631		761,904	1,639	763,543	763,543

(*Market Value of Investments on London Stock Exchange £792,002*)

	Current Assets :—			
33,135	Debtors and Payments in advance		41,581	
20,840	Cash at Bankers and in hand		12,732	
53,975				54,313
898,521				916,705

(*Note*: *See paragraph 5 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts*).

Quoted Investments and Uninvested Cash relating to Bequest Funds :—

		Quoted Investments at cost	Uninvested Cash		
9,342	Jenner Memorial Studentship Fund	8,545	875	9,420	
7,935	Morna Macleod Scholarship Fund	7,606	671	8,277	
498	Bacot Bequest Fund	—	—	—	
17,775		16,151	1,546	17,697	17,697

(*Market Value of Investments on London Stock Exchange £14,597*)

£916,296		£934,402

TO THE MEMBERS.

necessary for the purposes of our audit. In our opinion proper books of account have been kept by the Institute so Income and Expenditure Accounts which are in agreement with the books of account. In our opinion and to the tion given in paragraph 5 of the Financial Report of the Governing Body give the information required by the nstitute's affairs as at 31st December, 1950, and the General Fund Income and Expenditure Account gives a true

COOPER BROTHERS & CO.,
Chartered Accountants.

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1949)		
£		£
39,318	Salaries and Wages	41,014
2,143	Emoluments of two members of the Governing Body in an Executive capacity ...	4,475
1,359	Premiums on Federated Superannuation Policies	1,377
—	Premium on Group Pension Policy...	1,965
2,205	Rent, Rates and Insurance	2,577
4,890	Gas, Water, Fuel and Electricity	5,244
1,315	Office Expenses, Stationery and Printing	1,522
157	Auditors' Fee	157
360	Travelling Expenses	316
1,144	Biochemical Expenses	1,838
757	Bacteriological, Experimental Pathology and Nutrition Expenses	833
370	Biophysics Expenses	1,164
8,484	Serum, Vaccine and Vaccine Lymph Expenses	8,998
5,939	Animals	7,268
4,525	Animal House Expenses and Forage	6,627
6,727	Buildings, Alterations, Repairs and Renewals	18,864
1,376	General Apparatus and New Installations	4,326
470	Library Expenses	782
342	General Stores	1,280
70	Staff Canteen Loss	338
65	Amount written off Leasehold Property	65
2,916	Amount transferred to Sinking Fund for Freehold Buildings (including £2,611 Interest on Investments)	3,085
3,029	*Surplus* transferred to Contingency Reserve after charging £11,006 for additions to property and equipment included in the above expenses	15,036
£87,961		£129,101

PENSION

£		£
1,321	Pensions	1,654
285	Balance added to Fund	—
£1,606		£1,654

JENNER MEMORIAL

£		£
424	Stipend of Student	212
—	Balance added to Fund	78
£424		£290

MORNA MACLEOD

£		£
—	Stipend of Student	100
209	Balance added to Fund	117
£209		£217

for the year ended 31st December, 1950.

Fund.

(1949) £		£	£
	Interest on Investments (gross):		
21,013	General Fund	21,815	
2,492	Sinking Fund	2,611	
			24,426
55,976	Sales of Sera, Vaccines, Vaccine Lymph, &c.		97,108
8,480	Rent		7,567
£87,961			£129,101

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
—	Balance Deducted from Fund	48
£1,606		£1,654

Studentship Fund.

£		£
290	Interest on Investments (gross)	290
134	Balance Deducted from Fund...	—
£424		£290

Scholarship Fund.

£		£
209	Interest on Investments (gross)	217
£209		£217

INVESTMENTS AT 31st DECEMBER. 1950.

GENERAL FUND.

Nominal Value		Balance Sheet Value	Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	£82,000
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	41,965
£52,000	4 per cent. Funding Stock, 1960-90	45,662	55,770
£64,000	3½ per cent. War Stock, 1952, or after	63,408	60,320
£25,000	2½ per cent. Funding Loan, 1956/61	24,750	24,937
£20,000	2½ per cent. National War Bonds, 1951/53	20,000	20,225
£31,000	,, ,, ,, ,, 1952/54	31,000	31,504
£45,000	,, ,, ,, ,, 1954/56	46,595	46,350
£35,000	3 per cent. Savings Bonds 1955/65	35,000	35,437
£78,000	,, ,, ,, 1960/70	78,122	77,025
£10,000	,, ,, ,, 1965/75	10,000	9,700
£55,495	British Transport 3 per cent. Guaranteed Stock, 1978/88	55,495	50,779
£20,000	,, ,, ,, ,, ,, 1967/72	20,259	19,000
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	4,111
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77	1,898	1,925
£15,000	,, ,, 3½ ,, ,, ,, 1976/79	14,925	15,450
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75	2,687	2,895
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65	21,989	25 375
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	21,532
£2,900	Commonwealth of Australia 3½ per cent. Stock, 1950/52	2,724	2,958
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74	12,121	11,460
£25,000	,, ,, ,, 3 per cent. Registered Stock, 1965/67	19,800	24,375
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	932
		£645,644	£666,025

SINKING FUND FOR FREEHOLD BUILDINGS.

£10,200	4 per cent. Funding Stock, 1960-90	9,079	10,989
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	19,731
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	3,544
£3,700	,, ,, ,, 1960/70	3,709	3,654
£31,600	,, ,, ,, 1965/75	31,600	30,652
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	2,060
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	2,272
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77	6,460	6,160
£3,000	,, ,, 3 ,, ,, ,, 1968/73	2,916	2,903
		£80,717	£81,915

PENSION FUND.

£22,000	4 per cent. Funding Stock, 1960-90	17,165	23,595
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173	17,325
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	2,172
£1,000	3 ,, ,, ,, 1965/75	1,000	970
		£35,543	£44,062

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705	3,003
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88	1,986	1,817
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures	2,757	2,226
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after	1,097	1,073
		£8,545	£8,119

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, 3rd Issue	1,000	1,000
£500	3 per cent. Savings Bonds, 1960/70	500	494
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	4,118
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77	903	866
		£7,606	£6,478

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,
1951.

Chelsea Bridge Road,
London, S.W. 1.

June 14th. 1951.

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Gillian M. Harris, B.Sc. (*Research Student*).
M. J. Crumpton, B.Sc. (*Research Student*).
E. F. Annison, B.Sc., Ph.D. (*Agricultural Research Council Grantee*).
E. M. Thain, B.Sc., Ph.D., A.R.I.C. (*Department of Scientific and Industrial Research Grantee*).
Winifred M. Watkins, B.Sc., Ph.D. (*Medical Research Council Grantee*).
R. A. Gibbons, B.Sc. (*Medical Research Council Student*).
A. P. Mathias, B.Sc. (*Medical Research Council Student*).
Y. E. S. Gabr, B.Sc. (*Egyptian Government Student*).
J. D. Feinberg, M.S., Dr. V. M. (*U.S.A.*).
J. F. McCrea, M.A.Sc., Ph.D. (*Australia*).
Naomi Datta, M.D., Dip. Bact.
D. A. L. Davies, B.A.

NUTRITION.

Harriette Chick, D.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
B. Cinader, B.Sc., Ph.D., (*Beit Memorial Research Fellow*).
J. W. Lyttleton, M.Sc., Ph.D. (*New Zealand*).

BLOOD PRODUCTS RESEARCH UNIT.

Margaret E. Mackay, M.Sc., Ph.D. (*Medical Research Council External Scientific Staff*).
Margaret Nance, M.Sc. (*Medical Research Council External Scientific Staff*).
L. Vallet, B.A.
H. R. F. Arnstein, B.Sc.
§Jean Addey, B.Sc.
E. A. Caspary, B.Sc.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE).

W. d'A. Maycock, M.B.E., M.D., (*Superintendent of Elstree Laboratories and Estate*).
G. F. B. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc. (*Research Student*).

PREPARATION AND STUDY OF VACCINE LYMPH (ELSTREE).

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.B., B.S.
A. P. MacLennan, B.Sc. (*Morna Macleod Research Scholar*).

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†*Appointed Teacher of the University of London.*
**Recognised Teacher of the University of London.*
§*Working at Elstree.*

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE).

A. F. B. Standfast, M.A., Dip.Bact.
Margaret P. D. Pilr, B.Sc.
Dorothy H. Card, M.Sc.

Margaret E. Rowatt, B.Sc., Ph.D.
(Public Health Laboratory Service).
F. L. Masri, M.B., Ch.B. Dip.Bact.
(Egyptian Government Student).

BIOCHEMISTRY (ELSTREE).

D. E. Dolby, Ph.D.

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Blood Group Research Unit.

R. R. Race, Ph.D., M.R.C.S., L.R.C.P.
Ruth Sanger, Ph.D., B.Sc.
Helene A. Holt, B.A.
Joan S. Thompson, B.Sc.

Blood Group Reference Laboratory.

A. E. Mourant, M.A., D.Phil., D.M.
Dorothy M. Parkin, M.R.C.S., L.R.C.P.
Elizabeth W. Ikin, M.Sc.
Jean Walby, B.Sc.

ADMINISTRATION.

Secretary and Accountant - - - S. A. White, A.A.C.C.A.
Elstree Secretary and Estate Manager - F. K. Fox.

Solicitors:

Field, Roscoe & Co.,
52, Bedford Square, W.C.1.

Auditors:

Cooper Brothers & Co.,
14, George Street, Mansion House, E.C.4.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 14th. 1951.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report of the work of the Institute for the year 1950/51.

GOVERNING BODY.

As successor to Professor H. R. Dean, who had resigned owing to pressure of University work, the Council at its last meeting elected Sir William Wilson Jameson as one of its representatives on the Governing Body. The Council also re-elected Sir Henry Dale and Sir Paul Fildes as its other representatives until 31st. December, 1951.

The Governing Body takes pleasure in reporting that the honour of Knighthood was conferred on Dr. A. N. Drury in the King's Birthday Honours of 1950 and that he was recently elected a fellow of the Royal College of Physicians.

COUNCIL.

At last year's Annual General Meeting two of the three retiring members, Dr. J. Henderson Smith and Professor M. J. Stewart, did not seek re-election to the Council. The third retiring member, Professor S. P. Bedson, was re-elected. Dr. Muriel Robertson, Dr. A. A. Miles, Lord Balfour of Burleigh, Dr. J. E. McCartney and Dr. W. T. J. Morgan were also elected to the Council as representatives of the Members of the Institute

The three members of the Council due to retire this year in accordance with the Articles of Association but who are eligible for re-election, are Professor E. J. Conway, The President of the Royal College of Veterinary Surgeons and Professor H. R. Dean, representing the Royal Irish Academy, the Royal College of Veterinary Surgeons and the University of Cambridge respectively.

MEMBERS.

The Governing Body noted with pleasure that a member of the Institute, Professor T. Dalling, was knighted during the year.

The death of Lt.-Col. Glen Liston, a member since 1931, is recorded with regret.

Mr. A. F. B. Standfast has been elected a member of the Institute.

STAFF.

It is recorded with pleasure that Dr. P. Ellinger has recently been appointed Professor Emeritus and Ehrenbürger of the Academy, Dusseldorf.

Dr. D. E. Dolby and Miss D. H. Card have joined the Elstree Staff. Mr. S. A. White, formerly Assistant Secretary, was appointed Secretary in October. Mr. M. Crumpton and Mr. A. P. MacLennan were awarded a Research Studentship in Biochemistry and the Morna Macleod Scholarship respectively. Miss M. F. Kelleher, Miss J. Addey and Mr. E. A. Caspary have taken up temporary staff appointments.

Miss W. M. Stanier and Dr. D. Aminoff resigned during the year.

The Blood Products Research Unit, the Blood Group Research Unit and the Blood Group Reference Laboratory of the Medical Research Council are still accommodated at the Institute.

The Governing Body, before surveying the scientific work carried out during the year, desires again to record its appreciation of the continued co-operation and collaboration of the Medical Research Council with the Institute.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus pertussis. Mr. A. F. B. Standfast has continued his investigations into the antigens of *Hæmophilus pertussis.* A survey of the main characters of freshly isolated strains has shown that each of these characters can and does vary quantitatively and that they vary independently of one another. Therefore the presence of one character, even strongly marked, is not evidence that another character will also be strongly marked or even present at all.

The mouse protective antigen, which may well be the antigen responsible for the protection of children against whooping cough, can only be assigned by the somewhat complicated and time consuming mouse protection test. No satisfactory alternative test has been found. With this handicap the work of isolating and purifying the protective antigen must proceed slowly.

A serological investigation of strains of high and low agglutinability (within Phase I) has been started. Cross absorption tests have shown that only one major antigen is involved in these strains. A complicating factor is that either type of strain may be of high or low agglutinogen content as measured by quantitative absorption. It is hoped that this work will throw light on the mechanism of agglutination.

Dr. F. L. Masri has continued his investigation of the hæmagglutinin of *H. pertussis.* The conditions for its production in solid and liquid media have been studied. Extraction of the bacteria with sodium acetate followed by precipitation with cold methanol and absorption on to red blood cells has resulted in a purified preparation of the antigen in an active form, which has enabled some of the chemical, physical and biological properties to be investigated. The purest preparations appear to be free from other antigens. Preliminary tests suggest that the protective properties attributed to the hæmagglutinin have been due to contaminating antigens.

Dr. M. E. Rowatt has been investigating the amino-acid metabolism and growth requirements of *H. pertussis.* The oxidation of glutamic acid has been studied in particular and it has been shown that avirulent strains form a product which is not formed by virulent strains in quantities detectable under the conditions used. This compound has not yet been identified. It contains nitrogen but not sulphur and it is not a common amino-acid, a peptide or a volatile amine. Growth of avirulent strains of *H. pertussis* has been obtained in semi-defined media using small inocula.

Miss D. H. Card has started an investigation into the growth requirements of the murine strain of *Mycobacterium tuberculosis* (vole bacillus) with particular reference to liquid media.

Trichomonas Studies. The work on trichomoniasis in cattle has been continued by Dr. M. Robertson in collaboration with Dr. W. R. Kerr (Department of Veterinary Research, Ministry of Agriculture, Northern Ireland).

The studies on the inhibition of the skin reaction in animals sensitised to Trichomonas antigen have been continued. Various substances have been studied in addition to "phenergan," such as, sphingomyelin, cortisone and adrenocortico-tropic hormone. (A.C.T.H.)

Cortisone and "phenergan" (a synthetic antihistamine) have both been examined as regards their capacity, when mixed with the testing fluid, to prevent the local reaction in the skin. Phenergan when added to the testing fluid inhibits the reaction while cortisone does not.

The observations on the white corpuscle reaction and the accompanying desensitisation of the skin found during and immediately after parturition have been completed.

Work on the response of very young and old animals to vaccination with Trichomonas antigen is being continued.

Miss J. K. Clausen has continued her work on the growth of *Trichomonas fœtus in vitro.*

The metabolic end-products of *T. fœtus* have been investigated, the organisms being grown under semi-anærobic conditions. The acids present in the medium after growth have been extracted and identified by means of paper chromatography. Succinic and acetic acids were present in the used but not in the fresh medium.

The gas evolved by the organisms contains a high percentage of hydrogen and a little carbon dioxide. Little if any ammonia is produced. Tests for other nitrogenous end-products have not yet been made. The factors in serum essential for the growth of *T. fœtus* are heat-stable, water-soluble and non-dialysable. Other work has included testing the ability of different sugars to act as sources of carbohydrate, and the effect of oxygen tension in the atmosphere on growth.

Some comparative studies have been made with the flagellate *Strigomonas oncopelti.*

Mr. A. E. Pierce has commenced an electrophoretic and serological study of normal and immune bovine sera. Cattle and rabbits have been immunized with *Trichomonas fœtus* antigen. The normal and immune sera obtained from these animals have been examined and subjected to various methods of fractionation and absorption.

Experiments have also been carried out on the passive *in vitro* and *in vivo* sensitization of the guinea-pig uterus with immune sera prepared in the rabbit and bovine. Serum fractions prepared by salt fractionation have also been examined for their ability to fix passively in the guinea-pig uterus and produce a characteristic anaphylactic response in the Dale bath, and typical symptoms of anaphylaxis *in vivo*. Immune bovine serum and serum fractions have also been injected into calves, and intradermal tests carried out to detect any fixation of antibody in the dermis.

Experiments have also been started on the possible use of excised strips of the bovine uterus in the Dale bath.

Vaccinia Virus. In collaboration with Dr. E. Weston Hurst (Imperial Chemical Industries) Dr. D. McClean has continued his investigation into the possible relationship between "iso-allergic encephalitis" and post-vaccinial encephalitis. In the first experiment it was hoped, by very light sensitisation of guinea-pigs with both homologous and heterologous cerebral white matter with and without adjuvants, to show that subsequent vaccination precipitated paralytic symptoms and the typical histological changes in the central nervous system. The results were disappointing; there was no evidence that vaccination influenced the development of encephalitis. A second experiment with groups of guinea-pigs more thoroughly sensitised is now in progress. Lumsden's observation that many sensitised animals which manifest no paralytic symptoms, but nevertheless show the typical histological changes, has complicated the planning of the time intervals between sensitisation and vaccination, the selection of the optimum time at which to sacrifice for autopsy and the assessment of results.

Mr. L. Vallet and Dr. McClean have begun an investigation of the inactivation of vaccinia virus by ultra-violet light with a view to determining whether the treated virus is still antigenic. A preliminary dose of an antigenic preparation of killed virus might reduce the incidence of complications in those vaccinated for the first time at school age or in later life.

In collaboration with Dr. C. H. Lack (Royal National Orthopædic Hospital) and Professor R. H. Thompson (Guy's Hospital), Dr. McClean and Dr. L. H. Collier have continued their study of the influence of 2, 3- dimercapto-propanol (BAL) on the proliferation of vaccinia virus. The inhibition of virus lesions in the skin by inunction with BAL reported last year has been confirmed, but the interpretation of the results has been complicated by the gross variation in the copper content of the skin not only from rabbit to rabbit but also in different areas of skin in the same rabbit and also by the observation that although both sodium di-ethyl dithio-carbamate and 8-hydroxy-quinoline are even more effective than BAL in binding the copper in the skin, they completely fail to inhibit the virus lesion. Thus it appears that the action of BAL on the proliferation of the virus cannot be due to the removal of available copper. In order to determine how BAL acts on vaccinial infection, the action of the virus on intracellular enzyme activity is being investigated; in the first instance it has been shown by Warburg's direct method that the pyruvic oxidase activity of rabbit brain is increased when it is infected with vaccinia virus.

Dr. Collier is continuing his investigation into the conditions affecting the stability of vaccinia virus under different conditions of storage. It has been found that freeze-dried preparations of elementary bodies suspended in digest broth or in 1% peptone, and freeze-dried suspensions of vaccine pulp in distilled water hold their titre for long periods at room temperature, and deteriorate comparatively slowly at 37°C. Such preparations, together with a glycerinated suspension as issued for routine use, are being submitted to field trials on groups of hitherto unvaccinated children. In connection with this work, an examination is being made of the influence of flocculation of vaccinia virus on its infectivity.

Dr. Collier has elaborated a technique whereby infected chick embryos can be given repeated doses of chemotherapeutic agents by the yolk sac route, and will shortly conduct a series of experiments on the chemotherapy of vaccinia, using in the first instance a series of thiosemicarbazones.

Streptococcal Capsulation and Virulence. An attempt is being made by Mr. A. P. MacLennan in collaboration with Dr. McClean to define the conditions under which Group A and Group C streptococci produce capsules, both in culture and in animal body. The problem is being approached from two directions; the progressive simplification of broth media in which capsulation is maximal, and the step-wise elaboration of a simple defined medium in which capsulation does not occur. It has been found that capsule production by some Group A and Group C strains is not limited to serum-enriched media but occurs also in digest broth and even in peptone water.

The question whether capsule loss as cultures age is enzymic in nature, is under examination because of its bearing on the chemical relationship of capsular substance to the hyaluronic acid obtainable from streptococcal culture supernatants. Later work will aim at clarifying the relationship of capsulation to virulence.

Diphtheria antitoxin. Sir Percival Hartley has been investigating the properties of different kinds of homologous and heterologous diphtheria antitoxins. The whole natural serum, the β and γ globulins prepared by electro-phoresis, the globulins prepared by precipitation with neutral salts, and refined antitoxins prepared by the peptic digestion of diphtheria antitoxin (made, respectively, in the horse and in the guinea-pig) have been included in the studies. In comparative tests in guinea-pigs the behaviour of these different antitoxins towards toxin and towards virulent living cultures (the antitoxins being injected before or after the toxin or culture) has been studied.

The effect of peptic digestion on the properties of diphtheria antitoxin has been investigated; it has been found that, in addition to losing the property of passing the placental barrier and of sensitising guinea-pigs anaphylactically, the dispersal in the animal body, its retention and rate of elimination are very much altered after digestion with pepsin. An explanation for the changes produced by peptic digestion on the antitoxin molecule has been offered.

It has been shown that passive sensitisation *in vitro* can be effected and demonstrated by guinea-pig intestine as well as the uterus. Thus, the range and application of this method of study is greatly extended, as animals other than young virgin females can be used.

It has been shown that *gravis* strains of *C. diphtheriæ* isolated on Tyneside require more antitoxin for their control than certain other *gravis* strains and experiments have been conducted to see if a comparative test for virulence could be based on the observations.

Bacterial cytology. Dr. E. Klieneberger-Nobel has carried out an investigation both by phase contrast microscopy and in stained preparations of L-form production. It has been shown in *Hæmophilus Morax-Axenfeld* that prior to L-form production the bacterial filaments produce double spirals which bring different bacteria into juxtaposition. A fusion then takes place which is followed by L-form development. In *Proteus vulgaris* some filaments disintegrate under certain circumstances into granular forms which, it is suggested, by means of fusion likewise produce L-forms. In both cases the L-phase reproduces the bacillary phase. Dr. Klieneberger-Nobel is now engaged in a study of the effect of bacteriophage on L-form production.

Dr. R. G. Wittler has continued the study of the L-form of *Hæmophilus pertussis*. It has been found that the L-form retains to a large extent the virulence, toxicity, and serological specificity of the bacillary culture from which it is derived. Furthermore, it has been found that the L-form appears regularly in mice during the second or third week after intranasal inoculation with Phase I bacillary form of *H. pertussis*. The bacillary form is rapidly transformed into the L-form when injected into mice immunized with Phase I vaccine. L-forms isolated from the mouse revert to the bacillary form on Bordet-Gengou medium. The L-form of *H. pertussis* appears to be more resistant to ageing and the action of immune bodies than the bacillary form.

Specific antisera. Mr. G. F. B. Weitz has expanded his investigations on the preparation of specific precipitating antisera for identification tests on the blood meals of various blood-sucking insects so as to include a greater variety of mammalian species. To this effect studies were made on the presence of common antigenic factors in the serum protein of various mammals. By means of absorption technique, it was found that two types of antibodies are present in antisera prepared in rabbits. One type of antibody is characterized by its ability to

react with the serum proteins of all mammals and can be readily absorbed from the antisera with mammalian antigens. The second type of antibody complex reacts only with the serum proteins of mammals which are closely related to the species concerned. The latter type of antibody is difficult to remove by ordinary absorption methods but can be eliminated by cross immunisation experiments. Thus a highly specific antihuman serum was prepared in a chimpanzee which could be of great value for the distinction of serum proteins of man and higher apes in blood meals of tse-tse flies.

The work on feeding habits of *A. aquasalis* in Trinidad has been continued with Major R. A. Senior White, the Government malariologist, and well over 4,000 blood smears have been identified. Collaboration with workers in East Africa, involving identification of tse-tse fly meals, has increased as antisera against East African mammals becomes more available.

The possibility of using Azoproteins as labelling materials under experimental conditions for the identification of members of a single species is being investigated in collaboration with Dr. M. G. Macfarlane.

Plasma substitutes. Dr. W. d'A. Maycock and Miss L. Lorenz have investigated the renal excretion and disappearance from the blood stream of fractions of dextran of different average molecular weights: 22,000, 124,000, 220,000, 700,000, 3,000,000. The blood levels, in the first hour after injection, fall by some 40% to 60% except in the case of the smallest fraction. Only a small part of this fall is accounted for by renal excretion of the dextran, and hæmodilution due to the passage of tissue fluid into the circulation does not appear to be significant. In the case of the smallest molecular fraction, about 60% of the injected dextran is excreted within the first hour. After the first hour the curves of disappearance from the blood stream for all fractions are similar; the largest molecular fraction taking some six days to disappear, that of mol. wt. 124,000 some three days. The smallest molecular fraction is cleared from the blood stream within 24 hours. The excretion of dextran is accompanied in the first few hours by a diuresis, which is not detectable if 24 hour samples only are measured. Dextran can be detected serologically in the urine for several weeks after the plasma has been cleared of dextran.

It appears that in the first few weeks, after intravenous injection, the dextran which is not excreted, is distributed throughout all the tissues of the rabbit, including the brain, spinal cord, and cerebro-spinal fluid. The heaviest deposits are found in the liver. In heavily loaded animals dextran has been detected serologically in saline extracts of the following tissues: at six months after injection, brain, spinal cord, bone-marrow, lungs, liver, kidney, skeletal and cardiac muscle, stomach, lymph glands; at nine months after injection, cerebro-spinal fluid, bone-marrow, skeletal muscle, kidney, liver and lymph glands; at 12 months after injection, brain, cerebro-spinal fluid, liver, kidney and lymph glands.

Histological examination of the tissues of rabbits given various doses of the fractions mentioned above, and of dextran prepared for transfusion has been carried out in collaboration with Dr. R. Drury (University College Hospital) and has revealed no significant morphological changes attributable to dextran.

The excretion of dextran into the stomach has been studied in patients in collaboration with Dr. G. M. Bull (Post-graduate Medical School of London).

The examination of dextran used in the extended clinical trial under the ægis of the Ministry of Health and Medical Research Council has been completed.

The chemical methods used for the quantitative estimation of dextran have been further investigated. It has been shown that the Hint Thorsen Method which is used for the estimation of dextran in blood, is not reliable when large quantities of plasma or serum are used, and that the method cannot be used for the estimation of dextran in saline extracts of tissues. A method is being devised for the estimation of dextran in tissue extracts.

Slow constrictor substance in human serum. Mr. Y. E. S. Gabr, in collaboration with Sir Alan Drury and Dr. W. T. J. Morgan, has been investigating the chemical nature of the substance present in human serum which has a slow constrictor action on the guinea-pig's gut.

BIOCHEMICAL STUDIES.

The Blood Group Studies. Dr. E. F. Annison and Dr. W. T. J. Morgan have succeeded in isolating and characterising the gene product responsible for the "Lewis", Le^a, blood group character. The material is a mucoid very similar to the human group A-substance described earlier. The main components, fucose, galactose, glucosamine and chondrosamine and eleven amino-acids, appear to be common to both substances and further studies are being directed to determine the amounts of each of the components present in the group substances. Dr. Annison has carried out preliminary experiments on the oxidation of the Le^a substance with the periodate ion in order to compare the behaviour of this substance with that of the group A-substance under similar conditions.

Mr. R. A. Gibbons and Dr. Morgan have continued their attempts to isolate essentially homogeneous preparations of the human blood group B-substance from ovarian cyst fluids, but the difficulty of obtaining group B cyst fluids has considerably hindered the investigation and only limited progress can be reported. It seems probable that the group B material is composed of the same carbohydrate and amino acid residues as have already been reported for the group A and "Lewis" factors. The isolation of the human group B-substance as an essentially homogeneous material and the comparison of its properties with those of the human group A-substance is important as it will allow for the first time the products of allelomorphic genes to be compared.

Mr. M. J. Crumpton has undertaken the preparation of further specimens of the so-called O-substance which occurs in the tissue fluids and secretions of all secretors within the ABO blood group classification and in preliminary studies has commenced to investigate the action of enzymes obtained from *Cl. welchii* culture filtrates on this material.

Dr. Winifred Watkins and Dr. Morgan have completed their studies of the action of periodate on a number of different blood group receptors on the human erythrocyte surface. The relative susceptibility of the receptors to the action of periodate was measured by the loss of agglutinability with the homologous serum and by the fall in the power of the treated erythrocytes to absorb the corresponding antibody from solution. The M, N and *Rhesus* (D) receptors are readily destroyed during treatment with 0·001 *M* periodate at pH 5 for 15 minutes, whereas the A, B, H, P, Le^a and O receptors are not appreciably inactivated. Treatment of the red-cells with stronger periodate solutions at more acid pH, demonstrated that the "Lewis", Le^a, and group P factors are most resistant to oxidation with periodate. The investigation was undertaken in the hope that some insight would be gained into the nature of these blood group factors (M, N, P, *Rhesus* (D)), which do not occur in a water-soluble form and which up to the present have remained unidentified chemically; for various reasons it has not been possible to do this.

Dr. N. Datta is attempting to isolate from soil and from fermenting farm compost, micro-organisms which when grown *in vitro* will liberate into the culture fluid an enzyme which will decompose the human blood group substances.

Dr. J. F. McCrea and Dr. Morgan have collected from 50 litres of human group O erythrocytes about 1 g. of a lipo-carbohydrate material which possesses considerable group activity as well as a pronounced capacity to inhibit the agglutination of chicken red-cells by heated LEE influenza virus. Material isolated from group A_1B cells shows similar activity against the virus but displays no significant power to neutralise a human anti-O serum. Methods for the separation and purification of these two biologically active components of the erythrocyte extract are being devised.

Dr. McCrea has completed his studies on the physical and chemical properties of the mucoid which he has obtained from sheep submandibular glands and which has been shown to possess immense activity in the virus inhibition test. As little as 0·005 mg. of the purified mucoid completely inhibits 5 agglutinating units of heated influenza B (LEE) virus in the standard test with fowl erythrocytes. The material contains 10·3% N, yields 13·6% reducing sugars, as glucose, after acid hydrolysis and 12% chondrosamine, which is the only amino-sugar present.

Bacterial Antigens. Mr. D. A. L. Davies and Dr. Morgan have continued their work on the isolation and examination of the O somatic antigen of *Shigella shigae*. Evidence has been obtained that in some recent preparations of this material, enzyme degradation has occurred and has brought about important changes in the chemical nature of the native antigenic complex. The detection of these changes and the detailed examination of the resulting antigenic material, have caused considerable delay and little progress in this field of immuno-chemistry can be reported.

Dr. Datta has studied the immune response which arises in rabbits after the inoculation of 1μg. of a purified preparation of the O somatic antigen of *Shigella shigae*. Intravenous injection of the material gave a better response, as measured by the agglutination reaction, than antigen given subcutaneously. It was observed, however, that the number of doses administered had a greater influence on the antibody titres finally obtained than did the route of inoculation. The studies are being extended to include an examination of the formation of specific "Shiga" precipitins and lysins in these experimental animals.

Toxins and Enzymes. Dr. M. G. Macfarlane has continued a study of the biochemical factors involved in the action of the Clostridial toxins on cells or cell constituents which may determine the difference in virulence of the toxins on different species of animals. The action of *Cl. welchii* toxin on suspensions of mitochondria prepared from the liver tissue of mice, guinea-pigs and rabbits has been examined. These particles, which are lipoprotein in nature and carry many of the important enzymic activities of the liver cell, are readily attacked by the bacterial lecithinase, with a concurrent decrease in some of the enzymic activities. Detailed examination of the consequences of the toxic action on the succinoxidase activity of the mitochondria has revealed differences in the behaviour of mitochondria from different species of animals, those from mouse liver for instance, being much less affected than those from guinea-pig liver.

The probability that these differences reflect differences in the structure of the particle, which may be species-specific, is being investigated in collaboration with Dr. Datta by the preparation of immune sera.

Dr. Macfarlane and Miss G. M. Harris have examined the effect of *Cl. oedematiens* toxin on various isolated oxidation and glycolytic systems of muscle, without detecting any action which could account for the toxicity *in vivo*. The toxin, however, appears to have an inhibiting action in some circumstances on the cytochome oxidase of mitochondria, but the specificity and exact mode of this action has not yet been determined.

Studies on Coenzyme A. Dr. J. Baddiley and Dr. E. M. Thain have continued their studies on the structure of coenzyme A, the factor which participates in biological acetylation processes. This coenzyme is believed to be a dinucleotide composed of adenosine, pantothenic acid, a sulphur-containing substance (probably thioethanolamine) and two or three phosphate groups. The enzymatic degradation product of coenzyme A which is active in promoting the growth of *Acetobacter suboxydans* is now shown to differ from pantothenic acid $-2'$ or $-4'$ phosphate or the $2' : 4'-$ diphosphate, all of which have been synthesised. The behaviour of these phosphates towards acid and alkali has been investigated and conditions ascertained under which coenzyme A would give rise to these compounds if such groupings were present in its molecule. Methods have been developed for the separation and identification of the synthetic phosphates, their hydrolysis products and related substances on paper and it was found that acid and alkali hydrolysates of coenzyme A contain a compound indistinguishable from pantothenic acid $-4'$ phosphate. The presence in coenzyme A hydrolysates of adenosine $-5'$ phosphate and thioethanolamine has been confirmed and a tentative formula has been advanced.

Codecarboxylase. Dr. Baddiley and Dr. Thain, in collaboration with Dr. A. W. Rodwell of Cambridge, have proposed a new formula for codecarboxylase (pyridoxal phosphate). It was found that the intensity of the yellow colour of a suspension of a *Lactobacillus* producing codecarboxylase from pyridoxal was a good indication of the amount of coenzyme formed. The suggestion from these observations that natural codecarboxylase gives yellow solutions is supported by the marked yellow colour of synthetic pyridoxal phosphate in neutral solution. This colour, together with the absence of phenolic properties in the phosphate, is consistent with the presence in the molecule of a phosphorylated hydroxy-methylene-ketone structure. A formula incorporating this feature has been advanced.

Dr. Baddiley and Mr. A. P. Mathias are attempting a synthesis of the alternative phosphorylated hydroxymethyl structure.

Nucleosides. Adenine thiomethyl pentoside, the sulphur-containing nucleoside first isolated from yeast, has been shown by Dr. Baddiley to be 5'-deoxy$-5'$methylthio-9-β-D-ribofuranosyl adenine. This has been confirmed by synthesis. Starting from inosine, the

structure of which is fully established, a methylthio group was introduced by known chemical procedures into the terminal 5'-position of the sugar residue. The product was identical with hypoxanthine thiomethyl pentoside, obtained from the natural adenine nucleoside by deamination. Similarly, starting from adenosine a series of reactions led to the production of a 5'-methylthio derivative identical with adenine thiomethyl pentoside.

Hydrogenolysis of Thioamides. Dithioesters have been shown by Dr. Baddiley to give rise on hydrogenolysis with Raney nickel to hydrocarbons. Under similar conditions, however, thioamides behave in a more complex manner. In dioxan solution the expected secondary amides are formed, along with other unidentified products. In alcohol hydrogenolysis proceeds to the stage of hydrocarbon and amine, the latter then being ethylated by the solvent.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Equipment. Dr. J. W. Lyttleton has developed a diffusiometer for the measurement of the diffusion constants of macromolecules using an interferometric system of the Gouy type for the registration of the diffusion.

Dr. R. A. Kekwick, in collaboration with Messrs. J. & E. Hall, Ltd., Dartford, Kent, has been developing and testing a new design of freeze drying plant for the dessication of human plasma.

Electrophoresis and Ultracentrifuge Studies. In collaboration with Professor F. W. Rogers Brambell (University College of North Wales), Dr. Kekwick has been studying the changes in maternal sera and embryonic fluids in the rabbit following the injection of brucella antisera prepared in rabbits and bovines. The injections have been made in various sites, such as into the maternal circulation intravenously, and into the uterine lumen in order to discover the permeability of the various embryonic membranes to such agents and consequently the mechanism of the transfer of antibodies from mother to fœtus.

A number of human specific blood group substances, isolated by Dr. Morgan and his colleagues, have been examined. The results have influenced the methods of purification adopted. Some physico-chemical characteristics of purified products have been measured and it would appear that as a group the substances have a molecular weight of 260,000—300,000 and that the molecules are very asymmetrical in shape.

Dr. N. H. Martin (St. George's Hospital) has extended his work on pathological sera from patients with liver damage.

Immunological Studies. Dr. B. Cinader has been studying the inhibition of *Cl. Welchii* lecithinase by equine antitoxin with reference to the differentiation of activities of the beta and gamma antibodies, using a manometric method of estimation.

With Mr. Weitz work is continuing on the interaction *in vivo* of tetanus toxin and antitoxin in the mouse.

Ultra Violet Irradiation of plasma. In relation to the ultraviolet irradiation of plasma to inactivate the hepatitis factor, it has been claimed that the concomitant prolongation of clotting time was due to increased antithrombic activity. The effect has been studied by Dr. Lyttleton and Mr. Vallet, and it has been established that there is no increase in antithrombin following irradiation, but that the prolongation of clotting time is the result of modification of the plasma fibrinogen.

Human Plasma and Plasma Products. The Blood Products Unit, as in previous years, has prepared dried plasma, and plasma fractions for the Ministry of Health.

Mr. Vallet has developed apparatus for the sterilization of plasma with ultra violet light. The method is now in use in the routine production of dried plasma.

Miss M. Nance has continued her work on the fibrinogen fraction of human plasma.

Dr. M. E. Mackay has completed the work on the fractionation of bovine serum and plasma with ether. It has been found possible to separate beta globulin, gamma 1 and gamma 2

globulins from a mixture of beta-gamma globulins. A series of fractionations on plasma samples from individuals before and after immunisation with blood-group antigens has been carried out for Dr. P. L. Mollison (Medical Research Council Blood Transfusion Research Unit). In collaboration with Dr. Kekwick a method has been developed for the recovery of serum albumin, and work on the purification of albumin is in progress.

Dr. N. H. Martin has studied the calcium binding properties of protein fractions prepared in the Unit.

NUTRITIONAL STUDIES.

Heredity of the Nicotinamide methylating mechanism in rats. During the year Professor Ellinger's earlier results on the heredity of the nicotinamide methylating mechanism in rats have been considered statistically and additional information needed to complete the analysis has been obtained. It is not yet possible to summarise the results of the statistical analysis.

Observations on the effect of nitrogen mustard on the heredity of the nicotinamide methylating mechanism has been continued and extended to include the effect observed on female rats and on the later F generations of the offspring of nitrogen mustard treated males. The effect of nitrogen mustard treatment on females and their offspring seems to be far less distinct than on males. This might be due to the fact that the treatment causes either sterility within a few days of the treatment or, with smaller doses, no visible effect at all. The effect of the nitrogen mustard treatment on the later progeny of treated male rats seems to persist for at least six or seven generations.

The Metabolites of Nicotinamide. A new method for tracing unknown urinary metabolites on the basis of estimating extinction curves with a photo-electric photometer is in the course of development by Professor Ellinger and Miss M. F. Kelleher. The investigation is still in its preliminary stages.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Blood Group Studies. It seems beyond doubt that blood groups afford at present the most direct approach to the study of the human germ plasm. With this in mind the work of the Blood Group Research Unit is directed towards finding "new" blood group systems and towards filling gaps of knowledge in "old" ones.

The first problem is being approached by the testing of sera of persons known to have been immunized by pregnancy or transfusion. It is in such sera that antibodies defining "new" antigens have in the past usually been found. As a more active measure the Unit is giving small injections of blood to more than a hundred volunteers in the hope that some of them may respond by making antibodies to antigens yet unknown or only guessed at.

The following example shows what is meant by the filling of gaps in blood group knowledge. For six years there has been much argument whether the three pairs of the Rh complex are separable or not. Recently the Unit was fortunate in being sent a sample of blood from a person who, after much study, was found to lack two of the three parts, which parts are therefore evidently separable. Further, the missing antigens presumably reflect a small deletion in the Rh chromosome. Deletion is a phenomenon familiar in species which have been well studied genetically but no good case has previously been made for its occurrence in man.

The Unit has spent a good deal of time on the elucidation of the manner of inheritance of the blood group antigen called "Kidd" discovered in Boston, Mass.

Analysis of several hundred families, whose blood groups have been tested during the last four years, has made it seem very probable that the genes for the eight systems of blood groups are carried on different chromosomes. The ninth blood group system, Kidd, is being investigated from this point of view.

Dr. R. K. Waller of the Medical College of Virginia, Richmond, Virginia, and Miss Marion Lewis of the Children's Hospital, Winnipeg, Manitoba, have spent some months working in the Unit.

The Unit is in very close collaboration with Dr. A. E. Mourant of the Medical Research Council Blood Group Reference Laboratory. As in previous years much help has been given by Professor R. A. Fisher (Department of Genetics, Cambridge).

Blood Group Reference Laboratory. The Laboratory has continued to supply blood grouping serum of all kinds to the National Blood Transfusion Service and other users at home and abroad. It has had to face greatly increased demands for anti-A and anti-B grouping serum. The Transfusion Service has also increased its demands for sera of animal origin and for the standardization of Rh grouping sera and the investigation of routine serological problems, thus necessitating a further increase in the technical and maintenance staffs.

Examples of a great variety of hæmagglutinogens have continued to be found and made available for blood grouping purposes Quantities of sera both for routine issue abroad and for research purposes have been dried through the kindness of the Blood Products Research Unit. The Laboratory thus now holds dried qualitative standard preparations of nearly all known human blood group agglutinins.

Selected cases arising in the course of routine work have been studied in detail and papers prepared for publication. Anthropological blood group studies have been carried out on natives of Spain, the Canary Islands, Nigeria, Uganda, Kenya, India, Pakistan, New Guinea, Columbia and New Mexico.

Instruction has been given in blood grouping to about forty pathologists and techniciane from laboratories in Great Britain, the British Commonwealth and other places. Large numbers of tests have been done for laboratories in Europe and the British Commonwealth.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

HENRY H. DALE,

Chairman of the Governing Body.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1951.

FINANCIAL REPORT OF THE GOVERNING BODY.

1. The Balance Sheet for the year ended 31st December 1951 shows balances to the credit of the various funds as follows: Capital Fund £700,463; Specific Funds £120,848; Contingency Reserve £76,153 and Bequest Funds £17,896.

2. The Investments held in the General and Specific Funds and Bequest Funds showed a depreciation of £72,838 at the date of the Balance Sheet.

3. The General Fund Income and Expenditure Account shows the income for the year as £107,801 compared with £129,101 in 1950. Expenditure amounted to £120,491 against £114,065 last year. The deficit for the year is £12,690 compared with a surplus of £15,036 in 1950.

4. The year's deficit of £12,690 shown by the General Fund Income and Expenditure account has been written off against the Contingency Reserve.

5. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £8,282, £5,961 and £3,159 respectively.

6. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

H. H. DALE, *Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

15th May, 1952.

BALANCE SHEET

(1950) £		£	£
	Capital Fund:—		
	Donations, &c., received to date from the following:—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Berridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers' (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)	500	
21,097	Other Donations and Legacies (1891-1951)	21,172	
	General Fund Income and Expenditure Account Accumulated		
337,804	Surpluses as at 31st December, 1950 .. 337,804		
	Add Surplus on Investments sold .. 3,189	340,993	
697,199			700,463
	Specific Funds:—		
80,966	Sinking Fund for Freehold Buildings	84,091	
36,933	Pension Fund	36,757	
117,899			120,848
	Contingency Reserve:—		
	As at 31st December 1950	88,843	
	Less Deficit on General Fund Income and Expenditure Account, 1951	12,690	
88,843			76,153
908,941			897,464
	Current Liabilities:—		
11,992	Creditors and accrued charges	6,457	
772	Balance of Cancer Research Legacies (1937/50)	772	
—	Balance of Royal Society Grant (1951)	3,282	
12,764			10,511
916,705			907,975
	Bequest Funds:—		
9,420	Jenner Memorial Studentship Fund	9,710	
8,277	Morna Macleod Scholarship Fund	8,186	
17,697			17,896
£934,402			£925,871

H. H. DALE, *Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have examined the above Balance Sheet and annexed Income and Expenditure Account which are in all the information and explanations which we considered necessary for our audit. In our opinion these accounts ation required by the Companies Act, 1948, and show a true and fair view of the state of the Institute's affairs at

London, 19th May, 1952.

31st DECEMBER, 1951.

(1950) £		£	£	£
	Fixed Assets:—			
	FREEHOLD PROPERTY at cost:			
73,717	Land and Buildings, Chelsea	73,717		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,222	
	(*Note: Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	LEASEHOLD PROPERTY:—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,579		
155			90	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,849	(*Note: Additions and replacements since 31st December, 1920 have been charged to Revenue*)		—	98,784
	Quoted Investments and Uninvested Cash relating to General and Specific Funds:—			
		Quoted Investments at cost less amounts written off	Uninvested Cash	
645,644	General Fund	649,501		649,501
80,966	Sinking Fund for Freehold Buildings ..	80,717	3,374	84,091
36,933	Pension Fund	35,543	1,214	36,757
763,543		765,761	4,588	770,349	770,349
	(*Market Value of Investments on London Stock Exchange £696,456*)			
	Current Assets:—			
41,581	Debtors and Payments in advance			33,803
12,732	Cash at Bankers and in hand			5,039
54,313					38,842
916,705					907,975
	(*Note: See paragraph 5 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts*).			
	Quoted Investments and Uninvested Cash relating to Bequest Funds:—			
		Quoted Investments at cost	Uninvested Cash	
9,420	Jenner Memorial Studentship Fund	8,545	1,165	9,710
8,277	Morna Macleod Scholarship Fund	7,606	580	8,186
17,697		16,151	1,745	17,896	17,896
	(*Market Value of Investments on London Stock Exchange £12,618*)			
£934,402					£925,871

TO THE MEMBERS.

agreement with the books of account. In our opinion proper books of account have been kept. We have obtained amplified by the information given in paragraph 5 of the Financial Report of the Governing Body give the inform- 31st December, 1951, and of the deficit for the year ended on that date.

COOPER BROTHERS & CO.,

Chartered Accountants.

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1950) £		£
41,014	Salaries and Wages	44,289
4,475	Emoluments of two members of the Governing Body in an Executive capacity	5,256
1,377	Premiums on Federated Superannuation Policies	1,490
1,965	Premium on Group Pension Policy	2,708
2 577	Rent, Rates and Insurance	2,529
5,244	Gas, Water, Fuel and Electricity	6,145
1,522	Office Expenses, Stationery and Printing	1,654
157	Auditors' Fee	157
316	Travelling Expenses	426
1,836	Biochemical Expenses	3,420
833	Bacteriological, Experimental Pathology and Nutrition Expenses	430
1,164	Biophysics Expenses	776
8,998	Serum, Vaccine and Vaccine Lymph Expenses	11,282
7,268	Animals	6,013
6,627	Animal House Expenses and Forage	6,906
18,864	Buildings, Alterations, Repairs and Renewals	19,462
4,326	General Apparatus and New Installations	2,189
782	Library Expenses	779
1,280	General Stores	767
388	Staff Canteen Loss	628
65	Amount written off Leasehold Property	65
3,085	Amount transferred to Sinking Fund for Freehold Buildings (including £2,701 Interest on Investments)	3,125
15,036	*Surplus* transferred to Contingency Reserve	—
£129,101		£120,491

PENSION

£		£
1,654	Pensions	1,782
£1,654		£1,782

JENNER MEMORIAL

£		£
212	Stipend of Student	—
78	Balance added to Fund	290
£290		£290

MORNA MACLEOD

£		£
100	Stipend of Student	308
117	Balance added to Fund	—
£217		£308

for the year ended 31st December, 1951.

Fund.

(1950) £		£	£
	Interest on Investments (gross):		
21,815	General Fund	22,414	
2,611	Sinking Fund	2,701	
			25,115
97,108	Sales of Sera, Vaccines, Vaccine Lymph, &c.		74,621
7,567	Rent		8,065
—	Deficit transferred to Contingency Reserve after charging to Expenditure £19,235 for additions to property and equipment		12,690
£129,101			£120,491

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
48	Balance Deducted from Fund	176
£1,654		£1,782

Studentship Fund.

£		£
290	Interest on Investments (gross)	290
£290		£290

Scholarship Fund.

£		£
217	Interest on Investments (gross)	217
—	Balance Deducted from Fund...	91
£217		£308

INVESTMENTS AT 31st DECEMBER. 1951.

GENERAL FUND.

Nominal Value		Balance Sheet Value		Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	..	£72,000
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	..	35,752
£52,000	4 per cent. Funding Stock, 1960-90	45,662	..	51,220
£25,000	2½ per cent. Funding Loan, 1956-61	24,750	..	23,188
£64,000	3½ per cent. War Stock, 1952, or after	63,408	..	51,840
£35,000	3 per cent. Savings Bonds 1955/65	35,000	..	32,200
£78,000	,, ,, ,, 1960/70	78,122	..	68,055
£10,000	,, ,, ,, 1965/75	10,000	..	8,425
£55,495	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	55,495	..	43,009
£20,000	,, ,, ,, ,, ,, 1967/72 ..	20,259	..	16,000
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	1,898	..	1,670
£15,000	,, ,, 3½ ,, ,, ,, 1976/79 ..	14,925	..	13,425
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	3,480
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65 ..	21,989	..	22,875
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	17,617
£2,900	Commonwealth of Australia 3½ per cent. Stock, 1950/52 ..	2,724	..	2,929
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74 ..	12,121	..	9,900
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75 ..	2,687	..	2,535
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	..	792
£4,000	Bankers Investment Trust Ltd., Deferred Stock	7,806	..	6,800
£3,250	Debenture & Capital Investment Trust Ltd., Ordinary Stock ..	6,586	..	6,094
£1,125	General Consolidated Investment Trust Ltd., Ordinary Stock ..	2,359	..	2,306
£2,500	London & Montrose Investment Trust Ltd., Ordinary Stock ..	7,893	..	8,375
£2,500	London Scottish American Trust Ltd., Deferred Stock ..	6,942	..	7,000
£750	London Trust Co., Ltd., Deferred Stock	3,230	..	2,963
£1,090	Lowland Investment Co Ltd., Ordinary Stock	2,593	..	2,398
£3,750	Mercantile Investment & General Trust Co. Ltd., Ordinary Stock	13,401	..	10,875
£5,000	Rio Claro Investment Trust Ltd., Ordinary Stock	11,192	..	9,875
£2,500	River Plate & General Trust Co., Ltd., Deferred Stock ..	7,691	..	6,813
£3,500	Sphere Investment Trust Ltd., Ordinary Shares	8,211	..	7,000
£1,350	Standard Trust Ltd., Ordinary Stock	2,862	..	2,906
£5,000	Sterling Trust Ltd., Ordinary Stock	8,731	..	7,250
£6,000	Third Guardian Trust Ltd., New Ordinary Stock	7,913	..	6,930
£3,000	United States Debenture Corporation Ltd., Ordinary Stock ..	12,553	..	10,800
£4,000	Witan Investment Co. Ltd., Ordinary Stock	11,289	..	10,240
		£649,501		£585,537

SINKING FUND FOR FREEHOLD BUILDINGS.

£10,200	4 per cent. Funding Stock, 1960-90	9,079	..	10,017
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	..	16,810
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	..	3,220
£3,700	,, ,, ,, 1960/70	3,709	..	3,228
£31,600	,, ,, ,, 1965/75	31,600	..	26,623
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	..	1,993
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	..	1,920
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	6,260	..	5,344
£3,000	,, ,, 3 ,, ,, ,, 1968/73 ..	2,916	..	2,542
		£80,717		£71,727

PENSION FUND.

£22,000	4 per cent. Funding Stock, 1960-90	17,165 ..	21,670
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173 ..	14,760
£2,200	3 per cent. Savings Bonds, 1960/70	2,205 ..	1,920
£1,000	3 ,, ,, ,, 1965/75	1,000 ..	842
		£35,543	£39,192

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705 ..	2,758
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986 ..	1,589
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757 ..	1,762
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097 ..	891
		£8,545	£6,950

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, 3rd Issue	1,000 ..	1,000
£500	3 per cent. Savings Bonds, 1960/70	500 ..	436
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203 ..	3,480
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903 ..	752
		£7,606	£5,668

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,

1952.

Chelsea Bridge Road,
London, S.W. 1.

June 19th. 1952.

THE GOVERNING BODY.

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
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Clerk to the Governors ... W. d'A. MAYCOCK, M.B.E., M.D.

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THE STAFF.

DIRECTOR:

*Sir Alan N. Drury, C.B.E., M.A., M.D., F.R.C.P., F.R.S.

BACTERIOLOGY, SEROLOGY, and EXPERIMENTAL PATHOLOGY.

*Sir Alan N. Drury, C.B.E., M.A., M.D., F.R.C.P., F.R.S.
Muriel Robertson, M.A., D.Sc., LL.D., F.R.S. (*Honorary*)
Sir Percival Hartley, C.B.E., D.Sc., F.R.S. (*Grantee*).
Emmy Klieneberger-Nobel, Ph.D., D.Sc.
A. E. Pierce, F.R.C.V.S., M.Sc., D.V.S.M. (*Agricultural Research Council*).
Margaret E. Blewett, B.Sc. (*Agricultural Research Council*).
Jane K. Clausen, B.Sc. (*Agricultural Research Council*).

BIOCHEMISTRY AND IMMUNOCHEMISTRY.

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S. (*Professor of Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
*Marjorie G. Macfarlane, D.Sc., Ph.D.
*J. Baddiley, M.Sc., Ph.D.
P. Ellinger, D. Phil. and Med., F.R.I.C.
Mary F. Kelleher, B Sc. (*Research Student*).
Gillian M. Harris, B.Sc. (*Research Student*).
M. J. Crumpton, B.Sc. (*Research Student*).
E. M. Thain, B.Sc., Ph.D., A.R.I.C. (*Department of Scientific and Industrial Research Grantee*).
Winifred M. Watkins, B.Sc., Ph.D. (*Medical Research Council Grantee*).
R. A. Gibbons, B.Sc. (*Medical Research Council Student*).
C. J. M. Rondle, B.A. (*Medical Research Council Student*).
A. P. Mathias, B.Sc. (*Department of Scientific and Industrial Research Student*).
Y. E. S. Gabr, B.Sc. (*Egyptian Government Student*).
J. D. Feinberg, M.S., Dr. V. M. (*U.S.A.*).
D. A. L. Davies, B.A. (*Ministry of Supply*).
J. O'Dea, B.Sc. (*Australia*).
K. Knox, M.Sc. (*Australia*).

NUTRITION.

Harriette Chick, D.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).

BIOPHYSICS.

*R. A. Kekwick, D.Sc.
B. Cinader, B.Sc., Ph.D., (*Beit Memorial Research Fellow*).
E. A. Caspary, B.Sc.
N. H. Martin, M.A., B.M., B.Ch., B.Sc. (*Honorary Research Associate*).

BLOOD PRODUCTS RESEARCH UNIT.

Margaret E. Mackay, M.Sc., Ph.D. (*Medical Research Council External Scientific Staff*).
Margaret Nance, M.Sc (*Medical Research Council External Scientific Staff*).
L. Vallet, B.A.
§Jean Addey, B.Sc.
Shirley M. Evans, B.Sc.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE).

W. d'A. Maycock, M.B.E., M.D., (*Superintendent of Elstree Laboratories and Estate*).
G. F. B. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc. (*Research Student*).

PREPARATION AND STUDY OF VACCINE LYMPH (ELSTREE).

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.B., B.S.
A. P. MacLennan, B.Sc. (*Morna Macleod Research Scholar*).

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†*Appointed Teacher of the University of London.*
**Recognised Teacher of the University of London.*
§*Working at Elstree.*

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE).

A. F. B. Standfast, M.A., Dip.Bact.
Dorothy H. Card, M.Sc.
Kathleen Cook, B.Sc.
Margaret E. Rowatt, B.Sc., Ph.D.
(Public Health Laboratory Service).
Jean M. Horton, M.A., Ph.D.

BIOCHEMISTRY (ELSTREE).

*D. E. Dolby, Ph.D.

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL.

Blood Group Research Unit.

R. R. Race, Ph.D., M.R.C.S., L.R.C.P., F.R.S.
Ruth Sanger, Ph.D., B.Sc.
Joan S. Thompson, B.Sc.

Blood Group Reference Laboratory.

A. E. Mourant, M.A., D.Phil., D.M.
Dorothy M. Parkin, M.R.C.S., L.R.C.P.
Elizabeth W. Ikin, M.Sc.
Jean Walby B.Sc.

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Secretary and Accountant - - - S. A. White, A.A.C.C.A.
Elstree Secretary and Estate Manager - F. K. Fox.

Solicitors:

Field, Roscoe & Co.
52, Bedford Square, W.C. 1.

Auditors:

Cooper Brothers & Co.,
14, George Street, Mansion House, E.C. 4.

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*Recognised Teacher of the University of London.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 19th. 1952.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report of the work of the Institute for the year 1951/52.

GOVERNING BODY.

No change in the personnel of the Governing Body has taken place during the year. At its last meeting the Council re-elected Sir Henry Dale, Sir Paul Fildes and Sir Wilson Jameson as its representatives on the Governing Body until 31st December, 1952.

The Governing Body takes pleasure in recording the conferment of a viscountcy on Sir John Anderson in the New Year's Honours and of the title of Professor of Biochemistry on Dr. W. T. J. Morgan.

COUNCIL.

At last year's Annual General Meeting two of the three retiring members of Council, Professor E. J. Conway and the President of the Royal College of Veterinary Surgeons, were re-appointed. Professor E. B. Verney was later appointed by the University of Cambridge as its representative in succession to Professor H. R. Dean.

The three members of the Council due to retire this year in accordance with the Articles of Association but who are eligible for re-election are Professor T. J. Mackie and Mr. V. Zachary Cope, representing the University of Edinburgh and the British Medical Association respectively, and Dr. Muriel Robertson, a representative of the Members of the Institute.

The resignation from the Council of Dr. J. E. McCartney, who has gone abroad, has been received with regret.

It is recorded with pleasure that a member of the Council, Professor R. A. Peters, was knighted during the year.

The deaths of Professor J. W. Bigger, the representative of the University of Dublin, and of Professor H. S. Raper, who had worked at the Institute during the early years of the century and who had been a Member of the Institute since 1931 and of the Council since 1941, are recorded with regret.

MEMBERS.

The Governing Body noted with pleasure that a Member of the Institute, Dr. H. P. Himsworth, was created a K.C.B. in the New Year's Honours.

By the death of Sir Charles Sherrington, whose association with the Institute goes back to 1894, the Institute has lost a distinguished Member. In that year, as Professor Superintendent of the Brown Animal Institution, he co-operated with Dr. Armand Ruffer of the Institute in the production of the first antiserum against diphtheria to be made in this country. Sir Charles Sherrington had been a Member since 1918.

STAFF.

Mr. H. R. F. Arnstein resigned during the year. Miss S. M. Evans has taken up a temporary appointment with the Blood Products Unit.

Dr. J. Baddiley has been granted recognition by the University of London as a teacher in Organic Chemistry and Dr. D. E. Dolby as a teacher in Biochemistry.

Next year, when he has completed his distinguished term as Director, the Governors will be able more fully and appropriately to acknowledge the Institute's debt to Sir Alan Drury, for his devoted and effective discharge of the duties of that office. At the present stage they mention only, and with regret, the fact that the year under review is the last complete one of his tenure, and offer in advance a welcome to his successor, Dr. A. A. Miles, who is to take up his duties in October next.

The Blood Products Research Unit, the Blood Group Research Unit and the Blood Group Reference Laboratory of the Medical Research Council are still accommodated at the Institute.

The Governing Body, before surveying the scientific work carried out during the year, desires again to record its appreciation of the long standing and continued collaboration of the Medical Research Council with the Institute, as well as the more recently initiated location of certain items of research in the Institute by the Agricultural Research Council and the Department of Scientific and Industrial Research.

Apart from this support from the Public Funds, the Governors are able to welcome new evidence of the generous recognition which the achievements of the Institute, as a centre of medical and biological research, are receiving from charitable trusts and scientifically enterprising industry. The Royal Society of London, from trusts which it administers, has granted £3,500 towards the special equipment of a research on the chemistry of haptenes and antigens. The Nuffield Foundation has made two grants over terms of years—£3,000 annually for 5 years, for the support of Professor Morgan's immuno-chemical studies on blood groups, bacterial and protozoal antigens; and £1,000 annually for 3 years in support of Dr. Baddiley's investigations of a coenzyme. And, only recently, the Governors have gratefully concluded negotiations by which they have accepted a charitable endowment from Messrs. Arthur Guinness Son & Co. Ltd., for the establishment in the Institute of a Guinness-Lister Research Unit, to deal with a range of fundamental problems of microbial synthesis and general microbiology. A single grant of £10,000 is to be provided for initial equipment, and an annual grant of £10,000 for maintenance, for a period of 10 years in the first instance. To all those concerned with the support of the Institute's activities, from these various external resources, the Governors make grateful acknowledgment.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Hæmophilus pertussis. Mr. A. F. B. Standfast has continued his investigations into the antigens of *Hæmophilus pertussis*. The role of various antigens and some fractions, isolated from *H. pertussis,* is being followed by studying the antibodies formed in rabbits immunized with these fractions.

Dr. F. L. G. Masri has concluded his investigation of the hæmagglutinins of *H. pertussis*. In the purest form obtained the hæmagglutinin was unable to protect mice against infection by the intracerebral or the intranasal route. Rabbit serum prepared against the purified hæmagglutinin was unable to protect mice passively though it had a high neutralizing titre for hæmagglutinins *in vitro*.

Dr. M. E. Rowatt has continued her investigations into the amino-acid metabolism and growth requirements of *H. pertussis,* and has shown that certain rough strains of *H. pertussis* form ornithine and arginine during the oxidation of glutamic acid. These strains contain urease. Other rough strains and smooth strains do not have urease nor form ornithine and arginine from

glutamate although one of these compounds is generally present in cells harvested from solid media. The strains forming ornithine are not agglutinated by antisera against the other strains.

Certain growth factors have been shown to be required by rough strains grown in a partially defined medium.

Dr. J. M. Horton has started the chemical fractionation of *H. pertussis* with special reference to the "protective antigen." Various methods for isolating polysaccharides have been tried and some success has been obtained with a formamide extract. This extract will protect about 25% of mice against infection. Attempts are being made to increase its antigenicity. Experiments are in progress on a serological analysis to determine the correlation between the "protective" and other antigens.

Dr. D. E. Dolby has collaborated with Mr. Standfast in the production of a combined vaccine of protamine precipitated diphtheria toxoid and *H. pertussis* as an alternative to the use of alum precipitated toxoid, and has begun to collaborate with Mr. Standfast and Miss Horton in the study of the antigens of *H. pertussis* with special reference to the chemistry of the hæmagglutinins.

Vole Bacillus. Miss D. H. Card has continued her investigation into the growth requirements of the murine strain of *Mycobacterium tuberculosis* (Vole bacillus) and has started to investigate the drying of living vole vaccines from the frozen state with a view to the production of a stable potent vaccine.

Trichomonas Studies. Dr. M. Robertson has continued her study of trichomoniasis in cattle in collaboration with Dr. W. R. Kerr (Department of Veterinary Research, Ministry of Agriculture, Northern Ireland). The effect of A.C.T.H., cortisone, sphingomyelin, acetyl-sphingosine and the synthetic antihistamine phenergan in inhibiting the skin reaction in cattle sensitised to *trichomonas* antigen has been investigated. N-acetyl-sphingosine, recently isolated from crude sphingomyelin by Harington and Fisher, retains the desensitising effect of the crude product and has much the same order of potency as cortisone acetate of Merck. The lymphopœnia associated with the injection of A.C.T.H. and cortisone occurs also with sphingosine and the three substances are also alike in failing to produce the desensitisation effect until some hours after the injection. Phenergan has a different action and desensitisation is observed as soon as the injected drug itself is present at the site of the introduction of the specific testing fluid (hapten).

Work is in progress on a study of the elimination from the circulation of an antibody passively acquired from the colostrum in newly-born calves and the reaction of very young animals to injected antigen. Research is also being carried out on the origin of antibody found in the uterus of infected cattle and in animals where antigen has been introduced into the uterus.

Dr. J. D. Feinberg and Professor W. T. J. Morgan have completed their preliminary studies on the development of a method for the differential extraction of a specific substance from *Trichomonas fœtus*. Extraction of the freeze-dried organisms with anhydrous diethylenegycol results in the isolation of the specific substance essentially free from other material, in a yield of 1-2%. Further extraction with ethylenegycol gave a glycogen-like material, which was devoid of specific *T. fœtus* serological character. This substance is obtained in a yield of nearly 10% of the weight of the organisms used and is presumably a reserve carbohydrate. The purified specific substance has been used in extensive experimental work in cattle by Dr. W. R. Kerr and Dr. M. Robertson. It has proved to be a valuable reagent for experimental work on trichomoniasis and for studies on the fixation of anti-bodies in the skin and on desensitisation.

Mr. A. E. Pierce has continued the electrophoretic and serological investigation into normal and immune bovine sera and serum fractions.

The changes in the serum proteins following active immunization with *Trichomonas fœtus* during the period immediately before parturition, and upon subsequent calving are being studied.

The passive absorption of homologous and heterologous antibodies by the calf during the first twenty-four hours of life; their subsequent elimination, and the active development of serum proteins by the calf are also being investigated electrophoretically and serologically.

Miss J. Clausen has continued to work on the growth *in vitro* of the flagellates *Trichomonas fœtus* and *Strigomonas oncopelti*.

The glucose consumption of these organisms has been measured and correlated with the growth and pH curves of the cultures. The growth of *S. oncopelti* has been compared in the presence and absence of glucose. When glucose is available non-volatile fatty acids are produced as products of fermentation. In the absence of glucose ammonia production has been demonstrated.

Other work has included the investigation of serum as a source of growth factors for *T. fœtus*. Morphological studies of this organism have also been made.

Vaccinia Virus. The investigation by Dr. D. McClean in collaboration with Dr. E. Weston Hurst (Imperial Chemical Industries Ltd.) into the possible relationship between "iso-allergic encephalitis" and post-vaccinial encephalitis failed to establish any connection between these two conditions. There was no significant increase in the incidence of paralytic symptoms in those groups of guinea-pigs vaccinated after sensitisation with cerebral white matter with adjuvants compared with those sensitised pigs that were not subsequently vaccinated. Histological examination of the brains and spinal cords of the vaccinated and unvaccinated groups of animals also failed to reveal any significant difference in the incidence of demyelinating lesions.

Dr. McClean, Mr. L. Vallet and Dr. L. H. Collier are continuing their investigation into the antigenicity of vaccinia virus irradiated with ultra-violet light. Both vaccine lymph and purified elementary body suspensions have been irradiated and completely inactivated so far as can be judged by tests on the rabbit skin and in the embryonated egg. Groups of rabbits immunised with these preparations have developed a relative insusceptibility to vaccination as compared with normal rabbits and a significant rise in circulating virus neutralising antibody. Further experiments are necessary to ensure that this apparent antigenic activity of the irradiated material is not due to small doses of living virus undetected by the tests for inactivation. It is also necessary to find out for how long after immunisation the circulating antibodies can be detected. There is some evidence that the irradiated material deteriorates in storage. The antigenic stability of preparations dried from the frozen state is under investigation. If the preliminary results can be confirmed and extended it is hoped that a preliminary immunisation with irradiated virus may provide a basal immunity that will modify the reaction to subsequent vaccination with living virus and so reduce the incidence of complications, particularly of primary vaccination in later life.

Dr. Collier has almost completed his investigation into methods of preserving vaccinia virus at room temperature and at 37°C. Further experiments have confirmed the efficacy of peptone and digest broth as protective agents for freeze-dried vaccinia, and samples of virus dried in 1% and 5% peptone have been shown to retain some activity after more than two years' storage at 37°C.

The minimum dose of virus necessary to ensure 100% successful human vaccinations has been ascertained, with the object of defining the maximum permissible deterioration of freeze-dried vaccine stored at room temperature.

An investigation into the influence of freezing and drying on the physical state of vaccinial elementary bodies is in progress.

Bacterial Viruses. Dr. Dolby has continued studies on the reproduction of bacterial viruses which he was formerly pursuing at the University of Leeds. A survey has been made of the action of enzyme inhibitors on *Bact. coli.* B and the T series of bacteriophages to discover substances which differentially inhibit growth of either bacterium or phage, and it has been found that certain substances, such as arsenite and borate, as well as the acridine compounds already known to be active, will delay the multiplication of phage at concentrations which do not affect the growth of the bacteria. This inhibition is, however, only temporary. A compound which appears to have the opposite effect of inhibiting bacterial growth without altering that of the virus is sodium malonate.

Streptococcal capsulation and Virulence. Mr. A. P. MacLennan is continuing work on the factors controlling the production of hyaluronic acid by capsulated Group A and Group C

streptococci. In all strains examined a liberation of capsular hyaluronic acid into the culture medium occurs during the log phase of growth and is usually followed by rapid destruction of the polysaccharide. Although there is some indirect evidence that this destruction of hyaluronic acid may be due to the production of hyaluronidase in ageing cultures, so far no direct evidence of the presence of this enzyme has been obtained. Aeration of the culture of one Group C strain increases the amount of hyaluronic acid produced and delays its destruction; the possibility that this is due to the inhibition of enzymic action on the polysaccharide is being investigated. There is no simple relation between capsule size and the amount of hyaluronic acid produced.

Preliminary work on a partially defined medium suggests that acetate is effective in promoting continued growth on sub-culture of several Group A and Group C strains in this medium.

Diphtheria antitoxin. Sir Percival Hartley has been investigating the passage of different kinds of diphtheria antitoxin to the offspring and milk of actively and passively immunised pregnant and lactating guinea-pigs

When pregnant guinea-pigs are injected with diphtheria antitoxin of different kinds from different animal species there is at first a transfer of antitoxin to the serum of the mother. Homologous antitoxin passes more easily, and persists at a higher concentration and for a longer time, than heterologous antitoxin : the latter cannot be demonstrated, either in the mother's milk or the serum of the offspring, after a few days : the property of homologous antitoxin of passing to the milk or serum is very adversely affected and much reduced by peptic digestion.

The milk of guinea-pigs actively immunised against diphtheria antigens contains diphtheria antitoxin, the concentration being about one tenth of that of the serum : it is preserved at an almost unchanged, and usually high, concentration during lactation. Actively immunised mothers will "adopt" and suckle the young of normal animals; but evidence for the transference of diphtheria antitoxin by ingestion, in these or any other young guinea-pigs, has not been obtained; on the other hand, transference of antitoxin by the placental route in guinea-pigs can be shown and seems to be the natural method of antibody transfer in this species. By co-operation with Mr. Pierce, however, it has been shown that diphtheria antitoxin made in the horse, after ingestion by a day-old calf, appears in the serum of the calf a few hours later, and can be detected in the serum for several days. The offspring of actively immunised guinea-pig mothers contain diphtheria antitoxin usually at a somewhat higher concentration than their mothers, but this antitoxin appears to be "passive"; it varies in concentration in the young at birth, but it is lost after varying times afterwards.

Diphtheria antitoxin appears after injection in the milk of lactating guinea-pigs : again, homologous antitoxin passes to the milk more easily than heterologous antitoxin, persists longer at a higher concentration, and this property is almost lost after peptic digestion of the homologous antitoxin.

A further investigation of the most favourable conditions for the passive sensitisation, *in vitro*, of guinea-pig intestine with antibody, so that more extensive and more prolonged studies on the reaction to different antigens could be followed, has been conducted.

By co-operation with other members of the Institute staff, the production of human diphtheria antitoxin for therapeutic use and the changes in the electrophoretic pattern of the serum of human beings as a result of active immunisation against diphtheria, have been investigated. In association with Dr. W. d'A. Maycock and Dr. G. H. Tovey (S.W. Regional Blood Transfusion Centre, Bristol), diphtheria antitoxin of human origin has been obtained from actively immunised and re-immunised ("boosted") medical students in Bristol. It is proposed to estimate the antitoxin content of different batches of this material, to dry the plasma, and to use the material in cases of diphtheria. In association with Dr. R. A. Kekwick, the electrophoretic curves of the serum of five human subjects, before and after hyperimmunisation with diphtheria toxoid, have been determined. Arising out of this investigation, the local reaction following the intracutaneous injection of different kinds of diphtheria antigen has been followed in normal and immunised guinea-pigs.

Bacterial cytology. Dr. E. Klieneberger-Nobel has continued to study in detail the various ways of L-form production in bacteria. She is now engaged in an examination of Lederberg's so-called "sexual" strains derived from *E. coli*. K_{12}. She is following up the development of the zygotes and the connection of this phenomenon with the L-form production in bacteria.

Miss Wittler has brought to a conclusion her work on the L-form of *hæmophilus pertussis*.

Specific Antisera. Dr. B. G. F. Weitz has continued the study of the antigenic pattern of sera of human and animal origin. When sera are inoculated into rabbits a homologous and a heterologous antibody can be demonstrated in the antiserum; the characteristics of these antibodies have been determined by means of absorption tests and made it possible to formulate the antigenic make-up of the sera. The results of these experiments are being confirmed by anaphylactic tests by Sir Percival Hartley and Dr. R. I. N. Greaves (University of Cambridge).

The use of the "cross immunisation" technique has been employed on a large scale to prepare specific antisera against sera of various members of the family *Bovidæ*.

Thanks to the co-operation of Dr. C. H. N. Jackson (Acting Chief Entomologist, E.A.T.T.R.O. Shinyanga, Tanganyika), it has been possible to prepare antisera specific for the sera of *Impala* (Æpycerus melampus) and Reedbuck (Redunca redunca) in goats and sheep and for Buffalo (Syncerus caffer) in calves.

Further experiments are now in progress for the preparation of specific antisera against the sera of numbers of other bovids in calves, sheep, goats, and also in tropical animals, namely, Reedbuck, Dikdik and Duiker. Antisera prepared in this way have given completely specific results and will be used for the identification of blood meals of various tsetse flies.

Identification tests of blood meals of *A. aquasalis* have been continued and experiments are in progress to determine the longevity of blood meals in mosquitoes, mites, midges, lice and ticks, in co-operation with Professor P. A. Buxton (London School of Hygiene and Tropical Medicine).

Plasma substitutes. Dr. Maycock and Miss L. L. Lorenz have continued the investigation of the fate of dextran after intravenous injection. A method has been developed by Miss Lorenz for the determination of dextran in urine and aqueous tissue extracts, which permits the determination of 0·25 mg. dextran/ml. of urine and 0·1 mg. dextran/gm. of tissue (wet weight). The chemical and serological investigation of many tissue extracts awaiting examination has been started and it is evident that most of the dextran which can be recovered from the tissues is in the liver, bone-marrow, lymph glands and spleen.

Using the serological method for the detection of dextran the excretion of dextran in the urine of rabbits has been observed for long periods after dextran can no longer be demonstrated serologically in the plasma.

The reports received from hospitals using the dextran supplied by the Ministry of Health and Medical Research Council have been analysed. A number of sera from patients who have reacted to dextran infusion are under investigation.

Slow Constrictor Substance in Human Serum. Mr. Y. E. S. Gabr, in collaboration with Sir Alan Drury and Professor Morgan, has continued his investigations on the chemical nature of this substance. Various methods of purification have been tried and the possible relation of this substance to serotonin is being investigated. During one of the chemical procedures an active choline-like substance is produced; this is also being examined.

BIOCHEMICAL STUDIES.

The Blood Group Studies. Mr. R. A. Gibbons and Professor Morgan have found that certain mucoid materials obtained from secretions of persons belonging to group B are relatively inactive when titrated by the usual iso-agglutination inhibition technique using naturally occurring β-agglutinin but possess high activity when similarly tested against rabbit or human immune anti-B sera. The B substances isolated from three cyst fluids obtained from "secretors" belonging to group A_1B behaved similarly. Treatment of an essentially homogeneous human group B sub-

stance, which inhibited satisfactorily both normal and immune anti-B agglutinin, with a weakly alkaline buffer, pH 7.8, at 120° for a short time, gives rise to a material which possesses negligible activity when tested with natural β-agglutinin but retains full activity against both rabbit and human immune anti-B agglutinin. The chemical changes brought about by this treatment are being studied. The results indicate clearly the importance of examining serologically preparations of blood group B substance or their partial degradation products, with both natural and immune group agglutinins, before concluding that the specific serological B character is absent or has been lost during the isolation of the material.

Dr. Winifred Watkins has studied the reactivity of the O and H receptors on the surface of erythrocytes from group O cord bloods and the capacity of the saliva and meconium from newborn infants to neutralize human anti-O sera and anti-H reagents of human, animal and plant origin.

Professor Morgan and Dr. Watkins have found that the anti-H agglutinins in eel serum, an antibody frequently used to agglutinate O and A_2 cells preferentially, is inhibited in its action on O cells by the simple methylpentose, L-fucose. The examination of sugars possessing structures similar or closely related to that of L-fucose revealed that the most active derivative was *a*-methyl-L-fucopyranoside which, at a dilution of 1 :50,000, inhibited a standard agglutinating dose of the H serum. The implications inherent in the observation that simple sugars bring about inhibition can have practical significance since inhibition of the agglutination of cells by a naturally occurring heterologous serum which is brought about by biological materials of unknown composition, such as secretions or cell extracts, is usually interpreted as indicating the presence of a specific hapten or antigen. It is evident, however, that the observed inhibition may be due to the presence of a simple sugar and not to the specific hapten or antigen.

Mr. M. J. Crumpton and Professor Morgan have continued their studies on the enzymic decomposition of the human blood group substances. Using enzyme preparations of known specificity attempts have been made to identify the enzyme system responsible for the rapid decomposition of the group substances by filtrates from *Cl. welchii* type B cultures.

Mr. C. J. M. Rondle has studied the action of hypoiodite under strictly controlled conditions on the blood group mucoids, and has followed the oxidation of certain groups within these complex substances and determined the influences of the changes brought about on the serological properties of the materials.

Toxins and Enzymes. Dr. M. G. Macfarlane has continued her investigations on the effect of *Cl. welchii* toxin on the enzymic activities of mitochondria of liver and kidney. The systems studied, in addition to showing how this toxin may affect the metabolism of tissues, afford further evidence of the existence in mitochondria of some form of membrane limiting the access of substrates to the mitochondrial enzmyes, which has been suggested by other workers from electron microscope and other studies. Thus, in the absence of added cytochrome *c*, *p*-phenylenediamine but not ascorbic acid is utilised by the cytochrome oxidase system; this selective permeability is in some cases altered by treatment with *Cl. welchii* toxin, e.g., the permeability to β-glycerophosphate, indicated by the phosphatase activity, is increased.

Arising out of these findings, the capacity of the mitochondria in a suitable energy-producing system to concentrate ions selectively against a gradient is being investigated in conjunction with Dr. A. G. Spencer (University College Hospital).

Studies with Dr. N. Datta on the immunological specificity of liver and kidney mitochondria from rat and mouse failed to reveal any definite species or tissue specificity in these particles; Forsmann antigen was present in mouse but not in rat mitochondria.

Dr. Macfarlane and Miss G. M. Harris have investigated the lecithinase present in culture filtrates of *Cl. bifermentans,* to establish conclusively that this enzyme is of the same biochemical type as that of *Cl. welchii* toxin. The interest of this identity lies in the fact that the *Cl. bifermentans* enzyme has been shown by Miles and Miles to be non-toxic, in contrast to the *Cl. welchii* lecithinase which is highly toxic to many species of animals.

Miss Harris has also continued to examine the effect of *Cl. œdematiens* toxin on metabolic systems *in vitro.*

Coenzyme A. Chemical aspects of coenzyme A have been studied further by Dr. J. Baddiley and Dr. E. M. Thain. The cyclic pantothenic acid – 2′ : 4′ phosphate has been synthesised and found to differ quite markedly in its general properties from the 4′-phosphate and is not identical with a substance produced by alkaline hydrolysis of coenzyme A. However, under the conditions employed in the hydrolysis this cyclic phosphate is converted into the 4′-phosphate. Its failure to stimulate the growth of *A. subox.* eliminates it as a possible structural unit of the coenzyme. These studies have now been extended to the isolation, in sufficient amount for analysis and direct comparison, of certain degradation products of the coenzyme. An alkaline hydrolysate gave pantothenic acid – 4′ phosphate and also the cyclic phosphate. Purification of these fractions is in progress. The cyclic phosphate is an artifact, having arisen through intramolecular phosphorylation.

The position of the third phosphate group have been demonstrated at 2′ or 3′ in the adenosine moiety by periodate titration.

The preparation and chemical study of a number of thiolacetates supports the view that coenzyme A functions by accepting acetyl at its terminal SH group. The thiolacetates acetylated amines in dilute aqueous solution under very gentle conditions. In collaboration with Dr. Kekwick it has been shown that serum albumin can be acetylated with a thiolacetate on its free amino groups without degradation of the molecule.

A new and convenient synthesis of pantetheine (*Lactobacillus bulgaricus* factor) has been effected through β-alanyl-2-mercaptoethylamine.

Dr. Baddiley and Mr. A. P. Mathias are attempting the synthesis of a possible natural precursor of coenzyme A, namely, pantothenyl cysteine.

Codecarboxylase. Dr. Baddiley and Mr. Mathias have completed an unambiguous synthesis of codecarboxylase (pyridoxal phosphate). This synthesis shows, beyond doubt, that the phosphate group in pyridoxal phosphate is in ester linkage with the 5-hydroxymethyl group.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Equipment. A Spinco preparative ultracentrifuge has been installed in the Biophysics laboratory and has been used in the purification of specific blood group substances and bacterial antigens. The degree of purification achieved has been assessed by parallel measurements with the Svedberg ultracentrifuge.

Mr. E. A. Caspary has continued the development of the diffusiometer with the Gouy interferometric optical system. The apparatus is now in use for the measurement of the diffusion constants of macromolecules, though slight modifications are planned in the system on the basis of the experience obtained.

Mr. Vallet and Dr. Kekwick have been concerned with the design and testing of large-scale equipment for the aseptic fractionation of human plasma, in collaboration with Messrs. Aluminium Plant and Vessel Ltd.

Electrophoresis and Ultracentrifuge Studies. The studies of human specific blood group substances and bacterial antigens isolated by Dr. Morgan and his colleagues have been extended.

Dr. N. H. Martin has continued his work on pathological sera from patients with liver damage, and has also followed electrophoretically the changes occurring in the sera from these patients subsequent to their transfusion with human serum albumin provided by the Blood Products Unit.

Human Plasma and Plasma Products. Miss M. Nance and Dr. Kekwick have developed a method for the further purification of fibrinogen. A product has been obtained, virtually free from plasminogen and plasmin, which appears to be 97.5–98.5% clottable on a nitrogen basis. The ultimate level of clottability attainable is a matter of considerable interest in relation to the clotting mechanism. Such preparations will be used for physico-chemical characterisation measurements, and also in studies on the purification of plasminogen.

In collaboration with Dr. Dacie (Postgraduate Medical School) quantitative studies have been initiated by Dr. M. E. Mackay and Dr. Kekwick on the antihæmophilic globulin of normal human plasma. This material is precipitated almost completely in the crude fibrinogen fraction obtained from plasma by ether fractionation, and the fibrinogen purification procedure mentioned above may yield fractions of high antihæmophilic potency. No loss of activity occurs as a result of freeze drying crude preparations.

Immunological Studies. Utilising the inhibition of *Cl. welchii* lecithinase by equine antitoxin and antitoxic globulin fractions derived from it, Dr. B. Cinader has been able to make quantitative studies of the neutralisation curves and Danysz phenomenon in regions far removed from the neutral zone. The results can be interpreted in terms of the formation of a limited number of types of toxin-antitoxin complexes, and have an important bearing on the interpretation of dilution ratio data. The effect of removing the lipid from the antitoxin has also been studied.

In attempting to decide whether the enzyme inhibition is of a competitive or non-competitive nature, the inhibition of *cl. bifermentans* lecithinase by *Cl. Welchii* antitoxic globulins has also been examined.

Human Plasma and Plasma Products. The Blood Products Unit has continued the preparation of dried human plasma, and plasma fractions for the Ministry of Health.

Since the last report was made, two methods have been evolved by Dr. Kekwick and Dr. Mackay for the concentration of human serum albumin from the residues left after the globulins have been precipitated.

The limit of solubility of ether in aqueous solutions, which is reached at 19 volumes per cent. at – 3.5°C., made it difficult to precipitate albumin from the protein solution remaining after the removal of globulins from citrated plasma. The decisive factor is the low protein concentration. Recovery of 70-80% of the total protein was achieved by the addition to the globulin supernatant of ethyl alcohol to 25 volumes per cent., this with the ether already present bring the total solvent concentration to 34 per cent., at pH 5.0, Ionic strength 0.017, and – 5°C. The precipitate is soluble in water, and is 86% albumin, contaminated with alpha, beta, and gamma globulins.

The second method depends on the decrease in solubility of some proteins in combination with certain metal ions. It was found that the addition of zinc acetate to a concentration of 0.02 M at pH 5.5, I 0.037, and 18.5 volumes per cent. ether caused the precipitation of 80-86% of the total proteins of the globulin supernatant, the precipitate being 80% albumin.

Dr. Mackay has developed the method to separate the components of the crude albumin concentrates. As a result of these combined studies, three albumin preparations are now available. Crude albumin, precipitated by ethyl alcohol or zinc, which is essentially a concentration of the globulin supernatant. This crude albumin may be subjected to further fractionation when the globulin may be removed, leaving a solution which is 96% albumin and 4% beta globulin, and from this electrophoretically pure albumin may be obtained.

Enzyme studies showed that the bulk of the plasma choline esterase was concentrated with the crude albumin, and in further fractionations, with the globulins of this fraction. Work is in progress on the isolation and concentration of the choline-esterase rich protein. The work on choline esterase has been carried out with the collaboration of Dr. N. H. Martin and Mr. R. G. O. Kekwick (St. George's Hospital).

The crude albumin precipitated by alcohol and the 96% albumin have been used clinically by Dr. Martin.

Biological activity of certain plasma fractions. Sir Alan Drury and Miss M. W. Blewett have been examining the various plasma protein fractions for substances of biological interest, in addition to those known to be due to the protein constituent. One fraction constricts the guinea-pig's gut and also constricts the perfused mammalian vessels. (This is under examination by Mr. Y. E. S. Gabr). Attempts are being made to discover the source of origin of this substance. Another fraction inhibits the guinea-pig's and rabbit's gut, inhibits the rabbit's heart and constricts the perfused mammalian vessels. It is hoped that these observations may help to resolve the complexity of the effects of serum which have been known for many years.

NUTRITIONAL STUDIES.

Heredity of the nicotinamide methylating mechanism in rats. During the past year Dr. P. Ellinger has completed his experiments on the heredity of the nicotinamide methylating mechanism in rats. The results have now been analysed statistically and are being prepared for publication.

The detection of urinary metabolites by the spectrophotometer. A method has been developed by Dr. Ellinger and Miss M. F. Kelleher for tracing urinary metabolites by determining extinction curves of urine with a spectrophotometer. The method has been applied to the metabolites of salicylic acid and of nicotinamide. An unknown substance appearing in the urine after an oral dose of nicotinamide has been observed by this method and is now being isolated.

MEDICAL RESEARCH COUNCIL EXTERNAL SCIENTIFIC STAFF.

Blood Group Studies. The Blood Group Research Unit has continued to study blood groups from the genetical, as well as the serological viewpoint.

The attempt to immunize volunteers with small injections of blood has been continued; by this means it was hoped to stimulate antibodies for new blood group systems, and to fill in some of the antibodies missing from the systems already known. One hundred and twenty-five volunteers failed to make the desired antibodies.

A serum sent by Dr. Levine of New Jersey proved to be the first example of the anticipated anti-s, an antibody which we were trying to make in the volunteers. The inheritance of the antigen recognised by this antibody has been studied extensively. Anti-s makes the MNSs the most useful of all blood group systems in human genetics and problems of identity.

Many families have been tested to give further information on the inheritance of the more recently discovered blood group systems. Five hundred families have been analysed for linkage between the blood group genes, and from our results it seems probable that the genes for the nine blood group systems are carried on different chromosomes.

The Duffy system has been studied in a quantitative way by means of an anti-Fy^a serum which happily distinguishes the blood of homozygous Fy^aFy^a from heterozygous Fy^aFy^b people.

The Unit has continued to do blood groups for outside workers interested in twin studies, and in families with inherited abnormalities.

Recently the Unit has been investigating blood samples, sent by Professor Bhende of Bombay, which are disclosing a new allelomorph of the A_1 A_2 B O blood groups.

The Unit is in close collaboration with Dr. A. E. Mourant of the Medical Research Council Blood Group Reference Laboratory. As in previous years much help has been given by Professor R. A. Fisher (Department of Genetics, Cambridge).

Blood Group Reference Laboratory. The Laboratory has further increased its output of blood grouping sera of all kinds to meet the demands of users in Great Britain and abroad.

A hitherto unknown antibody in a serum sent from Berlin for investigation has been identified as the expected anti-Fy^b and an account has been published. Further investigations have also been made on a newly discovered blood group antigen in Africans.

Serum has been collected and tested in order to make National Standard preparations of anti-C, anti-D and anti-E.

In order to enable the Blood Transfusion Services to meet demands for special and rare groups, one hundred donors from each of the eighteen blood transfusion centres in Great Britain and Northern Ireland have been tested for all known blood groups (except Kidd). The results have been classified and supplies from any donor will be made available in any part of the United Kingdom where they may be needed.

Anthropological blood group studies have been carried out on persons from Borneo, the Channel Islands, India, Kenya, Nigeria, Tanganyika and Uganda.

Instruction to persons from laboratories in England and other countries has continued and specimens have been tested for, and serum supplied to, numerous laboratories abroad in order to help them in setting up their own testing services.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

H. H. DALE,

Chairman of the Governing Body.

SCIENTIFIC PAPERS PUBLISHED FROM THE LABORATORIES OF THE INSTITUTE DURING THE YEAR.

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BLOOD GROUP REFERENCE LABORATORY.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1952

FINANCIAL REPORT OF THE GOVERNING BODY

1. The Balance Sheet for the year ended 31st December 1952 shows balances to the credit of the various funds as follows: Capital Fund £700,463; Specific Funds £123,709; Bequest Funds £18,058 and Contingency Reserve £55,813.

2. The Investments held in the General and Specific Funds and Bequest Funds showed a depreciation of £84,369 at the date of the Balance Sheet for which provision has not been made.

3. The General Fund Income and Expenditure Account shows the income for the year as £103,532 compared with £107,801 in 1951. Expenditure amounted to £123,872 against £120,491 last year. The deficit for the year is £20,340 compared with a deficit of £12,690 in 1951.

4. The year's deficit of £20,340 shown by the General Fund Income and Expenditure account has been written off against the Contingency Reserve.

5. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £7,200, £5,307 and £3,132 respectively.

6. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

H. H. DALE, *Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

14th May, 1953.

BALANCE SHEET

(1951) £		£	£
	Capital Fund:—		
	Donations, &c., received to date from the following:—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Berridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers' (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)	500	
21,172	Other Donations and Legacies (1891-1951)	21,172	
	General Fund Income and Expenditure Account Accumulated		
340,993	Surpluses as at 31st December, 1951	340,993	
700,463			700,463
	Specific Funds:—		
84,091	Sinking Fund for Freehold Buildings	87,291	
36,757	Pension Fund	36,415	
		123,709	
	Bequest Funds:—		
9,710	Jenner Memorial Studentship Fund	10,000	
8,186	Morna Macleod Scholarship Fund	8,058	18,058
138,744			141,767
	Specific Grants and Legacies:—		
772	Balance of Cancer Research Legacies (1937-50)	772	
3,282	Balance of Royal Society Grant (1951)	2,905	
—	Nuffield Foundation Grant (1952)	3,000	
	Less Expenditure	924	2,076
4,054			5,753
	Contingency Reserve:—		
	As at 31st December 1951	76,153	
	Less Deficit on General Fund Income and Expenditure Account, 1952	20,340	
76,153			55,813
	Current Liabilities:—		
6,457	Creditors and accrued charges		11,321

H. H. DALE, *Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

£925,871	£915,117

REPORT OF THE AUDITORS

We have examined the above Balance Sheet and annexed Income and Expenditure Account which are in all the information and explanations which we considered necessary for our audit. In our opinion these accounts information required by the Companies Act, 1948, and show a true and fair view of the state of the Institute's

London, 19th May, 1953.

31st DECEMBER 1952.

(1951) £		£	£	£
	Fixed Assets:—			
	FREEHOLD PROPERTY at cost:			
73,717	Land and Buildings, Chelsea	73,548		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,053	
	(*Note*: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	LEASEHOLD PROPERTY:—			
	The Studio, Chelsea, at cost	2,669		
	Less Accumulated amounts written off	2,669		
90			—	
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,784	(*Note*: *Additions and replacements since 31st December, 1920 have been charged to Revenue*)		—	98,525
	General, Specific and Bequest Funds.			
	Quoted Investments at cost, less amounts written off and Uninvested Cash:—			

		Investments	Cash		
649,501	GENERAL	640,291	—	640,291	
~~84,091~~	SPECIFIC:				
84,091	Sinking Fund for Freehold Buildings ..	84,593	2,701	87,294	
36,757	Pension Fund	35,543	872	36,415	
	BEQUEST:				
9,710	Jenner Memorial Studentship Fund ..	8,545	1,455	10,000	
8,186	Morna Macleod Scholarship Fund ..	7,606	452	8,058	
788,245		776,578	5,480	782,058	782,058

(*Market Value of Investments on London Stock Exchange £693,209*)

	Current Assets:—			
33,803	Debtors and Payments in advance		33,079	
—	Bills Receivable		792	
5,039	Balance at Bankers and Cash in hand		663	
38,842				34,534

(*Note*: *See paragraph 5 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts*).

£925,871	£915,117

TO THE MEMBERS.

agreement with the books of account. In our opinion proper books of account have been kept. We have obtained amplified by the information given in paragraphs 2 and 5 of the Financial Report of the Governing Body give the affairs at 31st December, 1952, and of the deficit for the year ended on that date.

COOPER BROTHERS, & CO.
Chartered Accountants.

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1951)		
£		£
44,289	Salaries and Wages	48,415
5,256	Emoluments of two members of the Governing Body in an executive capacity	5,407
—	Gift to former Director	2,000
1,490	Premiums on Federated Superannuation Policies	1,584
2,708	Premium on Group Pension Policy	2,991
2,529	Rent, Rates and Insurance	2,273
6,145	Gas, Water, Fuel and Electricity	8,292
1,654	Office Expenses, Stationery and Printing	1,459
157	Auditors' Fee	157
426	Travelling Expenses	788
3 420	Biochemical Expenses	2,707
430	Bacteriological, Experimental Pathology and Nutrition Expenses	2,415
776	Biophysics Expenses	804
11,282	Serum, Vaccine and Vaccine Lymph Expenses	11,964
6,013	Animals	5,476
6,906	Animal House Expenses and Forage	7,371
19,462	Buildings, Alterations, Repairs and Renewals	11,642
2,189	General Apparatus and New Installations	2,326
779	Library Expenses	750
767	General Stores	1,050
—	Cost of New Lease	263
623	Staff Canteen Loss	444
65	Amount written off Leasehold Property	91
3.125	Amount transferred to Sinking Fund for Freehold Buildings (including £2,780 Interest on Investments)	3,203
£120,491		£123,872

PENSION

£		£
1,782	Pensions	1,948
£1,782		£1,948

JENNER MEMORIAL

£		£
200	Balance added to Fund	290

MORNA MACLEOD

£		£
308	Stipend of Student	345
£308		£345

for the year ended 31st December 1952.

Fund.

(1951) £		£	£
	Interest on Investments (gross):		
22,414	General Fund	24,836	
2,701	Sinking Fund	2,780	
			27,616
74,621	Sales of Sera, Vaccines, Vaccine Lymph, &c.		67,687
8,065	Rent		8,229
12,690	Deficit transferred to Contingency Reserve after charging to Expenditure £12,718 for additions to property and equipment		20,340
£120,491			£123,872

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
176	Balance Deducted from Fund	342
£1,782		£1,948

Studentship Fund.

£		£
290	Interest on Investments (gross)	290

Scholarship Fund.

£		£
217	Interest on Investments (gross)	217
91	Balance Deducted from Fund...	128
£308		£345

INVESTMENTS AT 31st DECEMBER 1952.

GENERAL FUND.

Nominal Value		Balance Sheet Value		Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	..	£69,600
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	..	34,444
~~£42,000~~	~~4 per cent. Funding Stock, 1960-90 .. ..~~	35,932	..	41,370
~~£25,000~~	~~2½ per cent. Funding Loan, 1956-61~~	24,750	..	23,375
£64,000	3½ per cent. War Stock, 1952, or after	63,408	..	49,920
£35,000	3 per cent. Savings Bonds 1955/65	35,000	..	32,550
£78,000	,, ,, ,, 1960/70	78,122	..	67,080
£10,000	,, ,, ,, 1965/75	10,000	..	8,400
£55,495	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	55,495	..	42,732
£20,000	,, ,, ,, ,, ,, 1967/72 ..	20,259	..	16,100
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	1,898	..	1,660
£15,000	,, ,, 3½ ,, ,, ,, 1976/79 ..	14,925	..	13,350
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	3,469
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65 ..	21,989	..	23,000
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	17,618
£2,900	Commonwealth of Australia 4½ per cent. Stock, 1960/62 ..	2,666	..	2,958
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74 ..	12,121	..	9,600
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75 ..	2,687	..	2,505
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	..	772
£4,000	Bankers Investment Trust Ltd., Deferred Stock	7,806	..	6,260
£3,250	Debenture & Capital Investment Trust Ltd., Ordinary Stock ..	6,586	..	6,012
£1,125	General Consolidated Investment Trust Ltd., Ordinary Stock ..	2,236	..	2,250
£2,500	London & Montrose Investment Trust Ltd., Ordinary Stock ..	7,893	..	7,500
£2,500	London Scottish American Trust Ltd., Deferred Stock ..	6,942	..	6,625
~~£750~~	London Trust Co., Ltd., Deferred Stock	3,230	..	2,921
£1,180	Lowland Investment Co. Ltd., Ordinary Stock	2,683	..	2,301
£5,625	Mercantile Investment & General Trust Co. Ltd., Ordinary Stock	13,401	..	11,109
£5,000	Rio Claro Investment Trust Ltd., Ordinary Stock	11,192	..	9,500
£2,500	River Plate & General Trust Co., Ltd., Deferred Stock ..	7,691	..	6,000
£3,500	Sphere Investment Trust Ltd., Ordinary Shares	8,211	..	6,300
£1,550	Standard Trust Ltd., Ordinary Stock	2,723	..	2,790
£3,000	Sterling Trust Ltd., Ordinary Stock	8,731	..	8,125
£3,750	Third Guardian Trust Ltd., New Ordinary Stock	8,663	..	8,809
£6,000	United States Debenture Corporation Ltd., Ordinary Stock ..	12,553	..	11,100
£4,000	Witan Investment Co. Ltd., Ordinary Stock	11,289	..	8,200
		£640,291		£566,305

SINKING FUND FOR FREEHOLD BUILDINGS.

£4,500	3 per cent. Funding Stock, 1959-69	3,876	..	3,915
£10,200	4 ,, ,, ,, 1960-90	9,079	..	10,017
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	..	16,195
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	..	3,255
£3,700	,, ,, ,, 1960/70	3,709	..	3,182
£31,600	,, ,, ,, 1965/75	31,600	..	26,544
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	..	1,975
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	..	1,856
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	6,260	..	5,312
£3,000	,, ,, 3 ,, ,, ,, 1968/73 ..	2,916	..	2,520
		£84,593		£74,801

PENSION FUND.

Nominal Value		Balance Sheet Value		Market Value
£22,000	4 per cent. Funding Stock, 1960-90	£17,165	..	£21,670
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173	..	14,220
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	..	1,892
£1,000	3 ,, ,, ,, 1965/75	1,000	..	840
		£35,543		£38,622

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705	..	2,758
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986	..	1,529
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757	..	1,789
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097	..	864
		£8,545		£6,940

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, 3rd Issue	1,000	..	1,000
£500	3 per cent. Savings Bonds, 1960/70	500	..	430
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	..	3,364
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903	..	747
		£7,606		£5,541

The Lister Institute
of
Preventive Medicine.

Report of the Governing Body,

1953.

Chelsea Bridge Road,
London, S.W. 1.

June 18th, 1953.

THE GOVERNING BODY

SIR HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S., *Chairman.*
THE RT. HON. VISCOUNT WAVERLEY, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., D.Sc., LL.D., F.R.S., *Hon. Treasurer.*
THE RT. HON. LORD BALFOUR OF BURLEIGH, D.C.L., D.L.
PROFESSOR S. P. BEDSON, M.D., B.S., F.R.C.P., D.Sc., F.R.S.
SIR PAUL FILDES, O.B.E., M.A., D.Sc., M.B., B.Ch., F.R.S.
THE RT. HON. THE EARL OF IVEAGH, C.B., C.M.G.
SIR WILLIAM WILSON JAMESON, G.B.E., K.C.B., M.A., M.D., F.R.C.P., LL.D.
A. A. MILES, M.A., M.D., F.R.C.P.
PROFESSOR W. T. J. MORGAN, D.Sc., PH.D., F.R.I.C., F.R.S.

Clerk to the Governors ... W. d'A. MAYCOCK, M.B.E., M.D.

THE COUNCIL

	REPRESENTING THE
PROFESSOR S. P. BEDSON, M.D., B.S., F.R.C.P., D.Sc., F.R.S.	Royal Society.
PROFESSOR EDWARD J. CONWAY, M.B., D.Sc., F.R.S. ...	Royal Irish Academy.
THE PRESIDENT OF THE ROYAL COLLEGE OF VETERINARY SURGEONS	Royal College of Veterinary Surgeons.
PROFESSOR E. B. VERNEY, M.A., M.B., B.CH., F.R.S. ...	University of Cambridge.
PROFESSOR D. WHITTERIDGE, D.M., B.Sc., F.R.S.	University of Edinburgh.
SIR V. ZACHARY COPE, M.S., F.R.C.S.	British Medical Association.
MURIEL ROBERTSON, M.A., D.Sc., LL.D., F.R.S. ...	Members of the Institute.
THE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS ...	Royal College of Surgeons of England.
PROFESSOR SIR RUDOLPH PETERS, M.C., M.A., M.D., F.R.S.	Members of the Institute.
PROFESSOR H. B. MAITLAND, M.D., M.R.C.S., L.R.C.P. ...	University of Manchester.
PROFESSOR SIR ALEXANDER FLEMING, M.B., B.S., F.R.C.S., F.R.S.	Members of the Institute.
SIR HENRY DALE, O.M., G.B.E., M.D. F.R.C.P., F.R.S. ...	" "
PROFESSOR SIR HOWARD W. FLOREY, M.A., PH.D., M.B., B.S., F.R.S.	University of Oxford.
PROFESSOR G. S. WILSON, M.D., B.S., F.R.C.P.	University of London.
...	Royal Agricultural Society.
SIR WILLIAM WILSON JAMESON, G.B.E., K.C.B., M.A., M.D., F.R.C.P., LL.D.	Members of the Institute.
PROFESSOR A. V. HILL, C.H., F.R.S.	" "
SIR ALAN N. DRURY, C.B.E., M.A., M.D., F.R.C.P., F.R.S.	" "
SIR EDWARD MELLANBY, G.B.E., K.C.B., M.D., F.R.S. ...	" "
DAME HARRIETTE CHICK, D.B.E., D.Sc.	" "
THE RT. HON. VISCOUNT WAVERLEY, P.C., G.C.B., G.C.S.I., G.C.I.E., M.A., D.Sc., LL.D., F.R.S. ...	" "
THE RT. HON. THE EARL OF IVEAGH, C.B., C.M.G. ...	" "
PROFESSOR S. R. K. GLANVILLE, M.A., F.S.A.	Worshipful Company of Grocers.
MAJOR L. M. E. DENT, D.S.O.	" "
PROFESSOR F. S. STEWART, M.D., B.CH., B.A.O.	University of Dublin.
THE PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS ...	Royal College of Physicians, London.
SIR CHARLES J. MARTIN, C.M.G., M.B., LL.D., F.R.S. ...	Members of the Institute.
THE RT. HON. LORD HORDER, G.C.V.O., M.D., B.Sc., F.R.C.P.	" "
A. A. MILES, M.A., M.D., F.R.C.P.	" "
SIR CHARLES HARINGTON, M.A., PH.D., F.R.S.	" "
SIR PAUL FILDES, O.B.E., M.A., D.Sc., M.B., B.CH., F.R.S.	" "
SIR PERCIVAL HARTLEY, C.B.E., D.Sc., F.R.S.	" "
THE RT. HON. LORD BALFOUR OF BURLEIGH, D.C.L., D.L.	" "
PROFESSOR W. T. J. MORGAN, D.Sc., PH.D., F.R.I.C., F.R.S.	" "

THE STAFF.

Director: A. A. Miles, M.A., M.D., F.R.C.P.

Deputy Director: Professor W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S.

BACTERIOLOGY, SEROLOGY, and EXPERIMENTAL PATHOLOGY.

*A. A. Miles, M.A., M.D., F.R.C.P.
Muriel Robertson, M.A., D.Sc., LL.D., F.R.S. (*Honorary*)
D. L. Wilhelm, M.D.
M. W. Schachter, M.D., M.Sc.
Emmy Klieneberger-Nobel, Ph.D., D.Sc.
Sir Percival Hartley, C.B.E., D.Sc., F.R.S. (*Grantee*).
A. E. Pierce, F.R.C.V.S., M.Sc., D.V.S.M. (*Agricultural Research Council*).

BIOCHEMISTRY

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S. (*Professor of Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
*Marjorie G. Macfarlane, D.Sc., Ph.D.
*J. Baddiley, M.Sc., Ph.D.
R. A. Gibbons, B.Sc., Ph.D.
M. J. Crumpton, B.Sc. (*Research Student*).
G. A. Jamieson, M Sc. (*Research Student*).
G. Owen, M.B., Ch.B., B.Sc. (*Research Student*).
Nina Czeczowiczka, B.Sc. (*Research Assistant*).
Marian Gibbons, B.Sc. (*Research Assistant*).
E. M. Thain, B.Sc., Ph.D., A.R.I.C. (*Imperial Chemical Industries Fellow*).
Winifred M. Watkins, B.Sc., Ph.D. (*Beit Memorial Research Fellow*).
J. G. Buchanan, M.A., Ph.D. (*Department of Scientific and Industrial Research Grantee*).
C. J. M. Rondle, B.A. (*Medical Research Council Student*).
A. P. Mathias, B.Sc. (*Department of Scientific and Industrial Research Student*).
Y. E. S. Gabr, B.Sc. (*Egyptian Government Student*).
J. D. Feinberg, M.S., Dr. V. M. (*U.S.A.*).
D. A. L. Davies, M.A. (*Ministry of Supply*).
J. O'Dea, B.Sc. (*Australia*).
K. Knox, M.Sc. (*Australia*).
L. Szabo, Dr. ès Sc. (*France*).

BIOPHYSICS

*R. A. Kekwick, D.Sc.
Margaret E. Mackay, M.Sc., Ph.D. (*Honorary*) (*Medical Research Council External Scientific Staff*).
B. Cinader, B.Sc., Ph.D., (*Beit Memorial Research Fellow*).
E. A. Caspary, B.Sc.
N. H. Martin, M.A., B.M., B.Ch., B.Sc. (*Honorary Research Associate*).

NUTRITION

Dame Harriette Chick, D.B.E., D.Sc. (*Honorary*).
E. Margaret Hume, M.A. (*Honorary*). (*Medical Research Council External Scientific Staff*).

BLOOD PRODUCTS

L. Vallet, B.A.
Margaret Nance, M.Sc (*Medical Research Council External Scientific Staff*).
§Jean Addey, B.Sc.
Shirley M. Evans, B.Sc.
J. D. Pearson, B.Sc.
Patricia Sheehan, B.Sc.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE)

*W. d'A. Maycock, M.B.E., M.D., (*Superintendent of Elstree Laboratories and Estate*).
B. G. F. Weitz, M.R.C.V.S.
Lisa L. Lorenz, B.Sc. (*Research Student*).

PREPARATION AND STUDY OF VACCINE LYMPH (ELSTREE)

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.D., B.S.
A. P. MacLennan, B.Sc. (*Morna Macleod Research Scholar*).

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†*Appointed Teacher of the University of London.*
**Recognised Teacher of the University of London.*
§*Working at Elstree.*

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE)

*A. F. B. Standfast, M.A., Dip.Bact.
Dorothy H. Card, B.Sc.
Kathleen Cook, B.Sc.
K. B. Linton, B.Sc.
Margaret E. Rowatt, B.Sc., Ph.D.
(*Public Health Laboratory Service*).
Jean M. Horton, M.A., Ph.D.

BIOCHEMISTRY (ELSTREE)

*D. E. Dolby, Ph.D.

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL

Blood Group Research Unit.

†R. R. Race, Ph.D., M.R.C.S., L.R.C.P., F.R.S.
Ruth Sanger, B.Sc., Ph.D.
Joan S. Thompson, B.Sc.

Blood Group Reference Laboratory.

†A. E. Mourant, M.A., D.Phil., D.M.
Dorothy M. Parkin, M.R.C.S., L.R.C.P.
Elizabeth W. Ikin, M.Sc.
Jean Graff, B.Sc.

ADMINISTRATION

Secretary and Accountant - - - S. A. White, A.A.C.C.A.

Elstree Secretary and Estate Manager - F. K. Fox.

Solicitors:

Field, Roscoe & Co.

52, Bedford Square, W.C. 1.

Auditors:

Cooper Brothers & Co.,

14, George Street, Mansion House, E.C. 4.

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*Recognised Teacher of the University of London.
†Honorary Member of Institute Staff.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 18th. 1953.

REPORT OF THE GOVERNING BODY.

The Governing Body has the honour to present its report of the work of the Institute for the year 1952-53.

GOVERNING BODY.

At its last meeting the Council re-elected Sir Henry Dale, Sir Paul Fildes and Sir Wilson Jameson as its representatives on the Governing Body until 31st December, 1953.

Dr. A. A. Miles, as Director, is now *ex-officio* a member of the Governing Body in place of Sir Alan Drury who resigned on 30th September last.

COUNCIL.

At last year's Annual General Meeting Dr. Muriel Robertson was re-elected as a representative of the Members. The British Medical Association re-appointed Mr. Zachary Cope as its representative and Professor D. Whitteridge was appointed to represent the University of Edinburgh in place of Professor T. J. Mackie who had resigned.

The three members of the Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are, the President of the Royal College of Surgeons and Professor H. B. Maitland representing the Royal College of Surgeons and the Victoria University of Manchester respectively, and Professor Sir Rudolph Peters, a representative of the Members of the Institute.

The Governing Body noted with pleasure that Mr. Zachary Cope was knighted during the year.

The death of Sir William Dampier, who had represented the Royal Agricultural Society since 1947, is recorded with regret.

MEMBERS.

During the year invitations to become Members of the Institute were accepted by Sir Hugh Beaver, Professor G. L. Brown, Professor E. J. King and Dr. C. J. Virden.

The Governing Body records with regret the deaths during the year of Dr. S. W. Allworthy, Dr. W. E. Gye, Dr. J. Henderson Smith and Dr. C. H. Kellaway. Dr. Allworthy was a Fellow of the College of State Medicine and became a Member of the Institute in 1894, when the College and the Institute (then the British Institute) amalgamated.

STAFF.

The retirement of Sir Alan Drury, announced in last year's Annual Report, took place on 30th September, 1952. At a meeting of the Governing Body it was resolved: "That on the retirement of Sir Alan Drury from the Directorship of the Lister Institute, the members of the Governing Body desire to express to him their deep sense of gratitude and admiration for the distinguished and devoted service which he has given to all the interests of the Institute and its staff during his term as Director. When Sir Alan accepted the appointment in 1943, in succession

to the late Sir John Ledingham, the governors were aware that they were entrusting the direction of the Institute's scientific programme and the responsible supervision of its affairs to one who had previously had no direct knowledge of its activities and its problems. They were the more impressed by the promptitude and quiet efficiency with which Sir Alan was able to assume the functions and responsibilities of the directorship and to become the trusted adviser of the Governors on all the matters of policy which have called for their decision during the difficult period of readjustment at the end of the war and during all the years that have followed.

Under Sir Alan's leadership the Institute has enjoyed a period of steady progress and well-planned development. Such changes and innovations as have been needed have been carried out with all proper consideration of special interests and traditions. He is leaving the Institute now, at a time when important new enterprises have been launched and others are in immediate prospect; and for these, and the outside support and interest which have made some of them possible, the Institute is especially indebted to Sir Alan's far-sighted initiative and enterprise and to his wisdom in negotiation.

Sir Alan takes with him the very hearty gratitude and good wishes of the Governing Body and all who have been in any capacity concerned with the affairs of the Institute during his Directorship. He leaves the Institute with its reputation enhanced and its activities expanding in the service of science and the community. The Governors hope that, during the years of activity yet before him, he will have a full enjoyment of the new opportunity which he has now accepted for research in a congenial and related field."

Sir Alan Drury has been succeeded as Director by Dr. A. A. Miles, formerly Deputy Director of the National Institute for Medical Research.

The Governing Body recognized the desirability of appointing also a Deputy Director of the Lister Institute, and they were glad to find that Professor W. T. J. Morgan was willing to add this contingent responsibility for the Institute to that which he has held so long, and with such distinction, as a departmental chief.

Dr. D. L. Wilhelm, Dr. M. W. Schachter and Mr. K. B. Linton have been appointed to the staff. Dr. Margaret Mackay, Dr. A. E. Mourant and Dr. R. R. Race were appointed Honorary members of the staff and Dr. R. A. Gibbons was also given a temporary staff appointment. Miss N. Czeczowiczka and Mrs. M. Gibbons have been appointed as Research Assistants and Dr. G. Owen and Mr. G. A. Jamieson have been awarded Research Studentships. Miss M. F. Kelleher and Mrs. G. M. Lewis completed the tenure of their studentships during the year.

The University of London have granted recogntion to Dr. Miles as a teacher of Pathology and Bacteriology and to Dr. W. d'A. Maycock and Mr. A. F. B. Standfast as teachers of Pathology and Bacteriology respectively.

Dr. P. Ellinger retired in June, 1952, and the Governing Body learned with regret of his death shortly afterwards.

The Blood Group Research Unit and the Blood Group Reference Laboratory of the Medical Research Council are still accommodated at the Institute. The Blood Products Research Unit has, as the Blood Products Laboratory, become one of the departments of the Institute.

Mention was made last year of grants over terms of years which had been made by the Nuffield Foundation, in support of a group of researches under Professor Morgan's direct leadership, and of another group, under Dr. Baddiley in the same Department. Abundant evidence will be found in the present Report of the fruitful researches which have already been financed from these most welcome benefactions. Acknowledgement is now due to the same Foundation for its further generous action, in making a grant of £3,000 per annum for five years, to provide for the financial needs of a scheme of researches under the personal leadership of the new Director, Dr. Miles, on natural chemical agents which affect the permeability of the endothelial walls of the capillary blood vessels, and contribute thus to the physiological and pathological vascular reactions to various kinds of irriation and injury.

Progress has also been made towards the effective opening of the Guinness-Lister Research Unit on Microbiology and the Governors are glad to be able to report that Dr. B. A. D. Stocker, of the Department of Bacteriology in the London School of Hygiene and Tropical Medicine, has accepted appointment as the first Head of the Unit.

BACTERIOLOGICAL, IMMUNOLOGICAL AND PATHOLOGICAL STUDIES.

Haemophilus pertussis antigens. Mr. A. F. B. Standfast has studied the effect of toxin by the intranasal and intracerebral routes in mice in an attempt to explain the difference in virulence of *H. pertussis* strains tested by these two routes. Toxin appears to play little part in virulence by the intracerebral route ; by the intranasal route it appears to be of considerable importance by reason of its ability to paralyse the cilia of the epithelium, and so enable the organism to make its primary lodgement in the lung.

Dr. J. M. Horton has continued her work on the chemical fractionation of *H. pertussis* to extract the protective immunizing antigen. Polysaccharides extracted by formamide, alone or in conjunction with globulin, proved to be inactive although preliminary experiments had indicated some activity. Fractional precipitation by ethanol from tryptic digests of the cells and soluble extracts from disintegrated cells, are being investigated.

The protective antigen, previously shown by Dr. Masry (1952 Report) to be distinct from the haemagglutinin and the toxin of *H. pertussis*, now appears to be distinct from the agglutinogen also. The protective action of rabbit antisera to the whole bacillus is unaffected by absorption with purified agglutinogen ; and purified agglutinogen will not immunize mice actively. Alkaline extracts of *H. pertussis* yield a polypeptide antigen that appears to be antigenically pure agglutinogen.

Variation in the potency of protective antisera with the route of administration of antiserum and infecting dose indicate that more than one type of antibody is concerned ; the rôle of antitoxin in protection against intranasal injections is under investigation.

Dr. M. E. Rowatt has worked on growth media for *H. pertussis* and allied organisms. *H. pertussis*, Phase I and IV, *H. parapertussis*, and two atypical *Haemophilus* spp. all use glutamic acid during growth, but whereas both phases of *H. pertussis*, after using up the glutamic acid of the medium remove certain other amino acids, the other organisms do not. In *H. pertussis*, Phase I, ammonia formation and glutamate removal are approximately equivalent in the early stages of growth *H. parapertussis*, *H. bronchisepticus* and the two atypical strains contain urease, but *H. pertussis* does not. *H. parapertussis* was the only species to form a brown pigment from tyrosine in washed suspension.

Sheep red blood corpuscles contain a growth stimulant for Phase I cells growing from small inocula in Cohen's medium, and the serum an essential growth factor for large inocula growing on Cohen's medium solidified by agar.

Miss K. Cook and Dr. Rowatt have investigated modifications of sheep blood Bordet-Gengou media and liquid media with a view to improving the protective potency of vaccines grown in them. The rôle and the strain of *H. pertussis* used, and the method of killing the cells, has also been studied.

Mr. Standfast and Miss K. Cook, in conjunction with Dr. J. O. Irwin of the London School of Hygiene and Tropical Medicine have continued their investigation of the mouse test for potency and whooping cough vaccines for the M.R.C. Whooping Cough Committee. Reasonably precise estimates of potency can be obtained only with eight replicate tests ; attempts to develop less expensive and time-consuming tests have been unsuccessful.

Vole Bacillus. Miss D. H. Card has continued her investigation of the growth requirements of the murine strain of *Mycobacterium tuberculosis* (Vole bacillus), and the drying of living Vole Vaccine from the frozen state, in order to produce a stable, potent vaccine.

Trichomonas Studies. Dr. M. Robertson has continued her study of *Trichomonas foetus* in cattle in collaboration with Dr. W. R. Kerr (Dept. of Veterinary Research, Ministry of Agriculture, Northern Ireland).

A study of the active and passive sensitisation of the uterus of the cow by *T. foetus* antigen has been completed. Active sensitisation occurs only when the *Trichomonas* or its antigen is introduced into the uterus itself. Antibodies in the blood circulating alone, produced by injection of antigen by other routes, do not sensitise the uterus. Passive sensitisation of the uterus could

be achieved only by local treatment; namely the instillation of a high titre antiserum against *T. foetus* into the uterus. The active sensitisation of the uterus appears to be due to the local production of antibody in response to the instilled antigens.

The fate in calves of maternal antibody to *T. foetus* and *Br. abortus*, acquired via the colostrum, has been investigated. The half life of the anti-bodies in the circulation of the calf varied between 15-50 days, depending on the dose of colostrum and the state of the animal; but in each animal the two antibodies disappeared at the same rate.

An example of "immunological paralysis" was discovered in the calf, in which large doses of *T. foetus* antigen before the 21st day of life, inhibited agglutinin production on subsequent reinoculation of antigen, when the animal was immunologically mature.

Dr. Jane K. Clausen completed her work on the growth *in vitro* of the flagellates *T. foetus* and *Strigomonas oncopelti*. The serum necessary for the growth of *T. foetus* can be replaced by a heat-stable extract of horse serum; the growth factors in the extract are under investigation.

Mr. A. E. Pierce has continued the electrophoretic and serological investigation of normal and immune sera, and fractions prepared by salt, alcohol and ether fractionation. Changes in the serum proteins of pregnant cows and heifers (normal and immunized) from 6½ months to the termination of pregnancy have been related to the development of antibodies in the udder. The immunological reactions of calves after the absorption of heterologous proteins with the colostrum and the possible passive transference of antibody from mother to foetus *in utero* are also being studied.

Dr. J. G. Feinberg has devised a medium for the bulk growth of bacteria-free *Trichomonas vaginalis* to provide material for isolation of the dominant antigen by methods used in earlier work with *T. foetus*. He has also investigated methods of isolation of *T. vaginalis* from clinical material.

Vaccinia Virus. Dr. D. McClean, Mr. L. Vallet and Dr. L. H. Collier have nearly completed their investigation of the antigenicity in monkeys and rabbits of vaccinia virus inactivated with ultra-violet light. Experiments in progress are designed to establish the fact that the consistent antigenicity of irradiated preparations is not due to traces of living virus that have escaped detection. The antigenicity of irradiated virus can be preserved for at least six months at 4°C. by drying the preparations from the frozen state; storage experiments at higher temperatures are in progress. Circulating antibody is detectable for at least twenty-two weeks after immunization with two spaced doses of irradiated virus, and a single subsequent reinforcing dose is followed by a secondary immune response. If the current experiments confirm that the results so far obtained are not due to traces of living virus, it is proposed to try this material on human volunteers, and to observe how far the reactions to subsequent vaccination with living virus are modified.

Dr. Collier has continued his investigation of methods of preserving vaccinia virus. Purified virus freeze-dried in 5% peptone is capable of yielding 100% successful primary vaccinations after storage for four months at 37°C. Such a vaccine can be manufactured economically, and is shortly to be used in a large scale trial in which the three Services are co-operating. Should this trial prove successful, it is hoped to issue dried vaccine to tropical countries in place of the lanolinated lymph used at present. The dried vaccine would also be useful for epidemic reserves. Other investigations by Dr. Collier have included the correlation of various methods of titrating vaccine, and a study of autointerference by this virus.

Bacterial viruses. Dr. D. E. Dolby has continued his work with the T series of bacteriophages in *Bact. coli B*. By applying a method of dilution of infected bacteria in saline, whereby intracellular bacteriophage is released, the course of inhibition of virus multiplication by enzyme inhibitors, such as arsenite and borate, has been studied. It has been confirmed that in conditions where the growth of the bacteria is unaffected by the inhibitors, multiplication of the bacterial virus may be delayed without affecting the final titre.

Streptococcal Capsulation. Continuing his work on streptococcal capsulation, Mr. A. P. Maclennan has obtained direct evidence for the presence of a hyaluronidase in cultures of a capsulated hyaluronic acid-producing C. streptococcus. It had previously been found that several

strains of group A and C streptococci produce hyaluronic acid which is destroyed in ageing cultures by a thermolabile agent. The hyaluronidase can be concentrated by protein precipitation of culture in serum-free media and the concentrate shows considerable activity by the standard methods of hyaluronidase assay. The pH optimum of 6.0 agrees with that of known streptococcal hyaluronidases although other evidence suggests that the enzymes may not be identical. In this group C strain the enzyme is produced from the early stages of growth onwards and the appearance of hyaluronic acid and capsules represents an excess of synthesis over destruction. The degree of aeration of the culture profoundly influences the relation of synthesis and destruction.

Diphtheria Antitoxin. Sir Percival Hartley has investigated the properties of different kinds of diphtheria antitoxin. Antitoxin produced in actively immunised guinea-pigs can be readily demonstrated in the milk of immunised mothers; it readily passes into the circulation of normal guinea-pigs on intraperitoneal injection, but not at all if it is fed, even from birth, when such antitoxin-containing milk is the only food the normal offspring receives.

Attempts were made to establish a colony of actively immunized guinea-pigs that had lost all circulating antitoxin, but not their basic immunity to the toxin, with a view to studying the immune state of the offspring. However, immunized mothers had antitoxin in high titre that was passed to litters in three successive pregnancies. The response to intracutaneous injection of different diphtheria antigens was studied in normal and immunized pigs, with a view to a simple method of testing antigens for their power to raise the immunity of immunized but "lapsed" animals, and for the absence of power to produce violent local reactions.

Microbiology. Dr. E. Klieneberger-Nobel has concluded her investigation of Lederberg's auxotrophic strains derived from *E. coli* "K12." Morphological evidence of sexuality in these strains, such as, for example, zygote formation, was not found. Dr. Klieneberger-Nobel is studying mixed infections in mice. Organisms of the pleuropneumonia group pathogenic for other animals are harmless when injected alone into mice, but with virus of ectromelia they aggravate the symptoms of this disease and themselves grow abundantly in the peritoneum and the organs of the mice. Non-pathogenic strains, however, are not potentiated by the virus.

Diagnostic Antisera for Insect Blood Meals. Mr. B. F. G. Weitz has continued his study of serological methods of identifying meals of blood sucking insects by precipitin tests in a large number of insects and ticks concerned with malaria, filariasis and relapsing fever from Kenya, Tanganyika, Nigeria, Trinidad and Mauritius.

Investigation of the specificity of the precipitin reaction in regard to the identification of serum proteins of closely related species were confirmed and a number of antisera were prepared in East Africa in bovids against the serum of other related bovids. The relatively low level of sensitivity obtained with some of these antisera was probably due to the similarity of the proteins involved. However, a large number of experimental feeds of *Gl. morsitans* were identified and the results are being studied in relation to the movements of the game in the area in which the flies were caught.

The specific inhibition of the agglutination by anti-protein sera of red blood cells treated with tannic acid and coated with serum proteins is being studied as an alternative to identification by the precipitin reaction.

Slow Constrictor in Human Serum. Mr. Y. Gabr has elaborated a method for the isolation of the smooth muscle slow contractile principle of human plasma. The active material appears to be a long-chain fatty acid. The isolated substance is markedly haemolytic for human red blood cells

Plasma Substitutes. Dr. W. d'A. Maycock and Miss L. L. Lorenz have continued the investigation of methods for the estimation of dextran, particularly in tissue extracts. It is evident that, within a few days of intravenous injections of dextran into the rabbit, in amounts comparable with those given in clinical practice, dextran is present only in the liver, spleen, lymph glands and bone-marrow, in quantities which can be measured chemically.

In order to study the total amount of dextran retained by the body, the disappearance of intravenously administered dextran was followed in mice; after a dose of 60mg./kg. about 5% remains in the mouse at 2 months and a trace after 4 months. Examinations were made of sera from normal individuals and from patients who had been given infusions of dextran, for precipitating and agglutinating antibodies to dextran or *L. mesenteroides*.

Experimental Pathology. Dr. A. A. Miles is studying the nature of the immunity of blood capillaries to the permeability-increasing action of histamine that is induced by prior treatment with histamine and histamine liberators; with special reference to the liberation of histamine in anaphylactic animals.

Dr. D. L. Wilhelm and Dr. Miles are investigating the changes in capillary endothelium and cement substance induced by histamine and other substances that increase capillary permeability.

In collaboration with Dr. M. E. Mackay, Dr. Wilhelm, Dr. M. Schachter and Dr. Miles are studying a large molecular substance found in alpha globulin fraction of guinea-pig serum that has proved to be a powerful inducer of increased capillary permeability in the guinea-pig.

Dr. Schachter is making a pharmacological survey of similar substances in the sera of various mammalian species with a view to correlating permeability factors with those responsible for the Brodie phenomenon.

BIOCHEMICAL STUDIES.

Human Blood-group Studies. Professor W. T. J. Morgan and Dr. W. M. Watkins have examined the reactivity of saline extract of certain plant seeds against human red cells of known phenotype and have studied the inhibition of these reactions by preparation of the human blood group substances and simple sugars of known constitution. The agglutinins present in *Lotus tetragonolobus, Laburnum alpinum* and *Cytisus sessilifolius* seeds reacted preferentially with group O cells and agglutination of these cells was inhibited by human and hog H-substance. The *Laburnum* and *Cytisus* agglutinins were not neutralised by any of the simple substances tested, but the *Lotus* agglutinin was inhibited by α-methyl-L-fucopyranoside to a higher titre than by the H-substance and was also neutralised to a lesser extent by other sugars possessing structures similar to that of L-fucose. The anti-A agglutinins extracted from *Vicia Cracca* and Lima bean seeds were inhibited by human A-substance and less strongly by N-acetylchondrosamine and methyl-N-acetylchondrosaminide. Extracts of *Sophora japonica* seeds agglutinated both A and B cells and absorption experiments indicated that the agglutinin reacts with a structure common to the A and B receptors. The agglutination of A or B cells by the *Sophora* extract was inhibited by either A or B substances and slight inhibition was also obtained with N-acetylchondrosamine and with sugars possessing related structures. These results lend support to evidence obtained from chemical investigations that L-fucose is of greater importance for H-specificity than for A and B specificity and suggest that the N-acetylchondrosamine configuration may play an important part in A-specificity.

Dr. Watkins has examined the action of cell free extracts of autolysed *Trichomonas foetus* cultures on the human blood group substances. Extracts of both *T. foetus* var. Belfast and *T. foetus* var. Manley have been found to contain enzymes which rapidly destroy the serological activity of A, B, H, Le^a and Le^b-substances. Similarly prepared extracts of the protozoa *Trichomonas vaginalis* and *Strigomonas oncopelti* were without action on the blood group mucoids. The properties of the enzymes present in the *T. foetus* extracts are being examined.

Mr. Knox and Professor Morgan have attempted to determine whether in secretions derived from "secretor" persons belonging to A_2, the specific determinant structures which are responsible for the A and H serological characters occur together on the same mucoid molecule or independently on separate molecules. Mucoid materials isolated from two ovarian cyst fluids belonging to the sub-group A_2 have each been fractionated from aqueous solution by the addition of alcohol or acetic acid. The ratio of the A and H serological character in the fractions, as determined by inhibition experiments, indicated that no part of the mucoid preparations possessed A or H activity alone. These investigations are being extended and an artificial mixture of mucoid materials, each of which possesses a single serological character (A or H), is being included for study

Dr. R. A. Gibbons has continued to study the chemical nature of the mucoid responsible for the group B serological character of human erythrocytes and secretions. A method for the determination of the amount and nature of the amino-sugars in the group substance has been investigated and the technique, which involves the use of an ion-exchange column, is being applied, in collaboration with Mr. Rondle, to study the separation of the amino-sugars present in other blood group substances.

Mr. O'Dea and Dr. Gibbons have elaborated a micro-method for the estimation of formaldehyde liberated during the oxidation of serine, simple carbohydrates and polysaccharides. After the removal of excess periodate and iodate by the addition of lead tetrathionate the addition of chromotropic acid gives rise to the formation with formaldehyde of a coloured complex which is quantitatively determined spectrophotometrically.

Dr. G. Owen has commenced work on the serology and immunochemistry of the "Lewis" blood group factors with the intention of characterizing more fully these interesting biological materials.

Mr. Crumpton and Professor Morgan have studied an enzyme system in culture filtrates of *Clostridium welchii* (Type B) which destroys the serological activity of human and animal blood substances. Considerable purification of the enzyme preparation has been achieved by its repeated fractionation from solution in weak phosphate-citrate buffer (pH 6.9: phosphate 0.05 M), by ammonium sulphate, and by dialysis against the same buffer at 2°C. The purified enzyme contains a β-galactosidase, a β-glucosaminidase, and a weakly reacting α-glucosaminidase but no α-galactosidase and reducing sugars are not liberated from methyl fucoside by the enzyme preparation.

The chemical changes associated with the enzymic degradation of homogeneous hog H substance have been investigated, using the enzyme preparation before and after heating at 55°C. for 10 minutes. The heated preparation is unable to destroy the serological activity or liberate reducing sugars from human A substance but is nevertheless more specific in its action on the H substance. Hog H substance treated with both enzyme preparations, loses its viscosity and serological activity, and fucose, N-acetylglucosamine, galactose and an N-acetylchondrosamine-galactoside are liberated. Similar experiments are being carried out with essentially homogeneous blood group substances of human origin.

Mr. C. J. M. Rondle has continued to study the oxidation of sugars and mucopolysaccharides by alkaline hypoiodite. Particular attention has been given to the conditions required to ensure quantitative and reproducible results and it has been found that a low temperature and carefully controlled pH are essential. The results of a similar investigation using blood group substances of both animal and human origin indicate that a small but definite amount of reducing sugar is present and that the reducing end-group is part of an amino-sugar. Further work is in progress to extend these observations and determine the precise character of the amino-sugar involved.

Toxins and Enzymes. Dr. M. G. Macfarlane, with Dr. A. G. Spencer (University College Hospital), has studied the osmotic properties of mitochondria isolated from rat liver by differential centrifugation. On incubation in a medium containing an oxidisable substrate, such as glutamate or succinate, with Mg ions, inorganic phosphate and adenylic acid, the mitochondria maintained a higher concentration of Na^+ and K^+ than that of the external fluid, and swelling was prevented. In the absence of adenylic acid, there was no concentration gradient, and swelling and agglutination of the mitochondria occurred. It is concluded that the secretory action is linked with the capacity for oxidative phosphorylation, in some way at present unknown. This study is now being extended to mitochondria from rat kidney.

Mrs. G. M. Lewis (née Harris) and Dr. Macfarlane continued studies with *Cl. oedematiens* toxin, in an attempt to find out the biochemical action of the lethal toxin. The action *in vivo* appears predominantly to be some effect on the vascular permeability causing oedema. The action of the toxin on the activity of respiratory enzymes and coenzymes, and of other enzymes such as choline esterase and carbonic anhydrase, which may be concerned in the maintenance of the normal permeability, was therefore examined, but no effect was observed which would account for the toxicity.

Coenzyme A. Dr. J. Baddiley and Dr. E. M. Thain have continued their study of the chemistry of coenzyme A. Two phosphate esters of pantothenic acid have been isolated from the products of alkaline hydrolysis of coenzyme A, and identified as pantothenic acid-4′ phosphate and pantothenic acid-2′: 4′ phosphate by comparison with the synthetic compounds.

Unambiguous syntheses of pantetheine-2′, -4′, and -2′: 4′ phosphates have been effected. A new method for the formation of cyclic phosphates has been discovered, and applied to the synthesis of pantetheine-2′:4′ phosphate. Professor Lipmann and co-workers in America have tested the synthetic phosphates of pantetheine and report that only the 4′ phosphate is active as a coenzyme A precursor in a liver enzyme system. This property is characteristic of a fragment of coenzyme A produced by enzymic fission of the pyrophosphate bond; therefore the activity of the synthetic compound provides convincing proof of the previously proposed structure for coenzyme A.

In collaboration with Dr. J. G. Buchanan experiments have been initiated with the object of synthesising the mixed pyrophosphate, b-dephospho-coenzyme A.

The biological origin of Coenzyme A was studied in a strain of *Lactobacillus arabinosus* which synthesises small amounts of CoA when incubated with pantothenic acid. If, in addition, cysteine is supplied, the capacity for CoA synthesis is greatly increased. Cysteine could not be replaced by 2-mercaptoethylamine, nor by a variety of other thiol compounds. However, pantetheine was more active than pantothenic acid plus cysteine. Pantothenylcysteine seemed the probable intermediate in the formation of pantetheine. Several methods for the synthesis of this compound were attempted by Dr. Baddiley and Mr. A. P. Mathias, and a route yielding a fairly pure product was discovered. A new method which it is hoped will obviate the difficulties experienced in these attempts, is under investigation. Pantothenyl-cysteine was only very weakly active in stimulating the synthesis of CoA. This indicates that cysteine is functioning as a specific source of sulphur. The following derivatives have been prepared: pantothenyl-2 hydroxyethylamine, pantothenyl-aminoacetaldehyde, pantothenamide, pantothenyl-α-and-β-alanine, pantothenyl-glycine, and pantothenyl-serine. Reports of the tests of pantothenyl-serine are not available. Pantothenyl-glycine was utilized by the organism for the synthesis of CoA. The remainder were inactive. A study of the mechanism by which pantothenyl-glycine (and serine?) is converted into pantetheine is planned.

Active Methionine. It has been shown recently that the coenzyme participating in biological transmethylation reactions in which methionine is the methyl donor is S-(5′-adenosyl)-methionine. Dr. Baddiley and Mr. G. A. Jamieson have obtained chromatographic evidence that thiomethyl-adenosine is one of the decomposition products of active methionine and are seeking to obtain this product in crystallisable quantities. An attempt to synthesise the inosine analogue of active methionine has also been initiated.

Penicillium islandicum polysaccharide. A polysaccharide material obtained by ferric chloride precipitation of the culture filtrate of *P. islandicum* has been examined by Drs. Baddiley, Buchanan and Thain. Contrary to expectation, it has been shown to be closely related to luteic acid, an acidic 1:6-β-polyglucose derivative previously obtained from *P. luteum*. Acid hydrolysis gave glucose as the only monosaccharide component. Malonic acid has been isolated from an alkaline hydrolysate, and titration of the polysaccharide indicated that the malonic acid was present as malonyl hemi-ester residues. The compound shows interesting colloidal properties in the presence of certain metallic salts.

Phosphorylation. The removal of phenyl groups from substituted phosphoric esters by sodium in liquid ammonia or organic bases is being investigated by Drs. Baddiley and Buchanan. The influence of a neighbouring hydroxyl or tosyloxy group on the lability of these esters is also being studied.

Transamination. The rôle of pyridoxal and pyridoxamine in the chemical interconversion of amino- and keto-acids has been studied by Dr. Baddiley. Co-ordination compounds between pyridoxal, metals and amines were isolated and it was shown that pyridoxal forms metallic

co-ordination compounds with many amino acids. A complex composed of one mol. pyridoxal, 1 mol. pyridoxamine, a metal, an amino acid and a keto-acid was proposed as an intermediate in metal-catalysed transamination. It was suggested that a similar complex may participate in biological transamination.

Toxoflavin. The yellow pigment of *Bacterium bongkrek* is highly toxic to animals. The structure proposed for this pigment, toxoflavin, bears a formal similarity to the purines and also to riboflavin. The possibility that it may inhibit competitively redox systems involving riboflavin is to be examined. Drs. Baddiley, Thain and L. Szabo are attempting to synthesise toxoflavin and analogous structures.

BIOPHYSICAL AND PHYSICO-CHEMICAL STUDIES.

Equipment. In collaboration with Messrs. J. & E. Hall, Dartford, Kent, Dr. R. A. Kekwick has completed developmental work on a new design of freeze drying plant to be used for the production of freeze-dried human plasma in the Blood Products Laboratory.

Diffusion, Ultracentrifuge and Electrophoresis Studies. Mr. E. A. Caspary has completed the construction of a diffusiometer with a Gouy interferometic optical system. Using this in conjunction with the ultracentrifuge he has studied the molecular kinetic properties of highly purified fibrinogen. There is evidence that the fibrinogen molecule may disassociate into smaller units in solutions containing less than 0.5 g. fibrinogen/100 ml.

In collaboration with Professor F. W. Rogers Brambell, F.R.S. (University College of North Wales) Dr. Kekwick has concluded a study of the embryonic fluids of the rabbit.

Blood Plasma Fractionation. Miss M. Nance is studying the purification of plasminogen from human plasma using the purified plasminogen free fibrinogen mentioned above as a substrate for assay purposes.

Immunological Studies. Dr. B. Cinader has continued investigations of toxin-antitoxin interaction, with special emphasis on the inhibition of *Cl. welchii* lecithinase by antibodies produced in the horse.

The inhibition of *Cl. bifermentans* lecithinase by *Cl. welchii* antitoxin was studied in two systems. In the first, enzyme and antibody were allowed to combine in the presence of substrate, and in the second in the absence of substrate. In the former case the course of the reaction is consistent with an enzyme-antibody combination ratio of 1.0.

Dr. Dolby is studying the fractionation of antitoxin horse sera and plasma by organic solvents with special reference to the antitoxic properties of the fractions isolated and the effect on them of the methods used in the large-scale preparation of antitoxic globulins. He is also investigating the kinetics of peptic activity under the conditions used in this process.

Human Plasma and Plasma Products. The Blood Products Laboratory has continued the preparation of dried human plasma and products derived from plasma fractions for the Ministry of Health.

In preparation for the move to new laboratories at Elstree a complete revision has been made of the techniques used to make the preparation and fractionation processes of the pilot plant stage suitable for large-scale work. The equipment for the ultra-violet irradiation of plasma has been improved, particularly with devices that ensure a uniform level of irradiation.

Dr. Mackay has continued her work on the separation by ether precipitation of the serum protein rich in pseudocholine-esterase. The enzyme activity was found to be quantitatively associated with the alpha globulin. A fraction consisting of 84% alpha globulin has been isolated, and is now being subjected to a further fractionation. This work has been carried out in collaboration with Dr. N. H. Martin, and Mr. R. G. O. Kekwick (St. George's Hospital).

Work is in progress on the sub-fractionation of human gamma globulins, with particular reference to the isolation and concentration of the blood grouping antibodies.

Blood Group Studies. The Blood Group Research Unit continues to study the genetical and immunological aspects of blood groups. New blood groups are being sought by investigating antibodies formed by transfused people, or by women who have had children suffering from haemolytic disease of the newborn. Many of the sera thought to contain a new antibody are found to contain mixtures of known antibodies.

Two new antibodies have been found, one of them, anti-Jk^b, in a serum sent by Dr. Gertrude Plaut of the North London Blood Transfusion Centre. An extensive study was made of a serum from Dr. P. Vogel and Dr. R. E. Rosenfield of New York, containing an antibody which shows the Rh groups to be yet more complex than appeared before.

An association has been demonstrated between the presence of anti-H in serum and the absence of A,B, or H antigens from saliva.

The Unit has collaborated with the late Dr. R. K. Waller in identifying the Rh genotype -D-/-D- in a white Virginian family. The only other example of this genotype was discovered by the Unit three years ago in a British family.

The Unit has collaborated with Dr. B. H. Kirman of the Fountain Hospital, Tooting, with Dr. J. N. Walton of the Royal Victoria Infirmary, Newcastle-upon-Tyne, and with Dr. Eliot Slater and Mr. J. Shields of the Maudsley Hospital, Denmark Hill, in twin investigations and searches for linkage between disease genes and blood group genes.

The Unit is in close collaboration with Dr. A. E. Mourant of the Medical Research Council Blood Group Reference Laboratory. As in past years, much help has been given us by Professor Sir Ronald Fisher (Department of Genetics, Cambridge).

Blood Group Reference Laboratory. The Laboratory has further increased its output of blood-grouping sera of all kinds to meet the demand of users in Great Britain and abroad. The Laboratory has now been recognised by the World Health Organization as the International Blood Group Reference Laboratory.

Sufficient of the anti-D serum has been collected for the establishment of National and International Standards. The results of grouping tests on 2,000 blood donors forming a National Panel have been classified. The first example of the expected anti-Fy^b was discovered and a second case of anti-Jk^a was found.

Anthropological blood group studies have been carried out on Lapps, Yemenite Jews, Northern Sudanese, the Ewe and Ashanti, the Nigerians, the Shona and the people of North-West Pakistan. A special survey has been made of the peoples of India and Africa ; and Miss E. W. Ikin in collaboration with Dr. H. Lehmann (St. Bartholomew's Hospital) has surveyed blood groups of the Andaman Islanders.

Extensive investigations have been made of two antigens, so far found only in negroes, which further subdivide the MNSs blood group system.

Dr. D. M. Parkin is working on a possible relationship between blood groups and the life-span of skin homografts, and a study of blood group antigens of familial occurrence.

Courses of instruction to persons from laboratories in England and other countries have been given ; and specimens have been tested for, and serum supplied to many laboratories abroad, to help them in setting up their own testing services.

The Governing Body are glad again to recognise the growing output of important and distinguished work from the different Departments and the devoted, loyal and co-operative effort by all the staffs of the Institute to which such a result bears witness. Such a healthy growth of activities, in a period of steeply rising costs inevitably gives cause for some anxiety on financial grounds; but the Governing Body will explore every possible source of such additional revenue as may be needed to meet any proper development.

H. H. DALE,

Chairman of the Governing Body.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1953

FINANCIAL REPORT OF THE GOVERNING BODY

1. The Balance Sheet for the year ended 31st December 1953 shows balances to the credit of the various funds as follows: Capital Fund £699,666; Specific Funds £131,683; Bequest Funds £18,215 and Contingency Reserve £44,716.

2. The Investments held in the General and Specific Funds and Bequest Funds showed a depreciation of £21,651 at the date of the Balance Sheet for which provision has not been made.

3. The General Fund Income and Expenditure Account shows the income for the year as £110,251 compared with £103,532 in 1952. Expenditure amounted to £121,348 against £123,872 last year. The deficit for the year is £11,097 compared with a deficit of £20,340 in 1952.

4. The year's deficit of £11,097 shown by the General Fund Income and Expenditure account has been written off against the Contingency Reserve.

5. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £7,544, £4,342 and £4,144 respectively.

6. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

20th May, 1954.

BALANCE SHEET

(1952) £		£	£
	Capital Fund :—		
	Donations, &c., received to date from the following :—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Berridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers' (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)	500	
21,172	Other Donations and Legacies (1891-1953)	22,035	
	General Fund Income and Expenditure Account Accumulated Surpluses as at 31st December, 1952 .. 340,993		
	Less Amount written off and loss on sale of investments 1,660		
340,993		339,333	
700,463			699,666
	Specific Funds :—		
87,294	Sinking Fund for Freehold Buildings 90,555		
36,415	Pension Fund 36,108		
—	Re-endowment Fund 5,020		
		131,683	
	Bequest Funds :—		
10,000	Jenner Memorial Studentship Fund 10,290		
8,058	Morna Macleod Scholarship Fund 7,925	18,215	
141,767			149,898
	Specific Grants and Legacies :—		
772	Balance of Cancer Research Legacies (1937-50) ..	772	
2 905	Balance of Royal Society Grant (1951)	2,492	
	Nuffield Foundation Grants (1952-3) 10,000		
2,076	*Less* Expenditure 6,194	3,806	
—	Guinness-Lister Research Grant (1953) 7,500		
	Less Expenditure 7,389	111	
5,753			7,181
	Contingency Reserve :—		
	As at 31st December 1952	55,813	
	Less Deficit on General Fund Income and Expenditure Account, 1953	11,097	
55,813			44,716
	Current Liabilities :—		
11,321	Creditors and accrued charges		11,697

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

£915,117	£913,158

REPORT OF THE AUDITORS

We have examined the above Balance Sheet and annexed Income and Expenditure Account which are in all the information and explanations which we considered necessary for our audit. In our opinion these accounts information required by the Companies Act, 1948, and show a true and fair view of the state of the Institute's

London, 24th May, 1954.

31st DECEMBER 1953.

(1952) £		£	£	£
	Fixed Assets:—			
	FREEHOLD PROPERTY at cost:			
73,548	Land and Buildings, Chelsea	73,548		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,053	
	(*Note*: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS:—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,525	(*Note*: *Additions and replacements since 31st December, 1920 have been charged to Revenue*)		—	98,525
	General, Specific and Bequest Funds.			
	Quoted Investments at cost, less amounts written off and Uninvested Cash:—			

		Investments	Cash		
640,291	GENERAL	620,917	—	620,917	
	SPECIFIC:				
87,294	Sinking Fund for Freehold Buildings ..	88,089	2,466	90,555	
36,415	Pension Fund	35,543	565	36,108	
—	Re-endowment Fund	4,941	79	5,020	
	BEQUEST:				
10,000	Jenner Memorial Studentship Fund ..	8,545	1,745	10,290	
8,058	Morna Macleod Scholarship Fund ..	7,606	319	7,925	
782,058		765,641	5,174	770,815	770,815

(*Market Value of Investments on London Stock Exchange £743,990*)

	Current Assets:—		
33,079	Debtors and Payments in advance	31,385	
792	Bills Receivable	4,148	
663	Balance at Bankers and Cash in hand	8,285	
34,534			43,818

(*Notes*: *See paragraph 5 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts.*

There is a contingent liability of £2,250 in respect of partly paid shares).

£915,117	£913,158

TO THE MEMBERS.

agreement with the books of account. In our opinion proper books of account have been kept. We have obtained amplified by the information given in paragraphs 2 and 5 of the Financial Report of the Governing Body give the affairs at 31st December, 1953, and of the deficit for the year ended on that date.

COOPER BROTHERS & CO.
Chartered Accountants.

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1952) £		£
48,415	Salaries and Wages	51,122
5,407	Emoluments of two members of the Governing Body in an executive capacity	5,478
2,000	Gift to former Director	—
1,584	Premiums on Federated Superannuation Policies	1,822
2,991	Premium on Group Pension Policy	3,361
2,273	Rent, Rates and Insurance	2,634
8,292	Gas, Water, Fuel and Electricity	7,787
1,459	Office Expenses, Stationery and Printing	1,436
157	Auditors' Fee (Two years)	315
788	Travelling Expenses	875
2,707	Biochemical Expenses	1,739
2,415	Bacteriological and Experimental Pathology Expenses	918
804	Biophysics Expenses	680
11,964	Serum, Vaccine and Vaccine Lymph Expenses	13,431
5,476	Animals	6,731
7,371	Animal House Expenses and Forage	7,396
11,642	Buildings, Alterations, Repairs and Renewals	9,139
2,326	General Apparatus and New Installations	1,218
750	Library Expenses	789
1,050	General Stores	749
263	Cost of New Lease	—
444	Staff Canteen Loss	473
91	Amount written off Leasehold Property	—
3,208	Amount transferred to Sinking Fund for Freehold Buildings (including £2,856 Interest on Investments)	3,260
£123,872		£121,348

PENSION

£		£
1,948	Pensions	1,913
£1,948		£1,913

JENNER MEMORIAL

£		£
290	Balance added to Fund	290

MORNA MACLEOD

£		£
345	Stipend of Student	350
£345		£350

for the year ended 31st December 1953.

Fund.

(1952) £		£	£
	Interest on Investments (gross):		
24,836	General Fund	24,423	
2,780	Sinking Fund	2,836	
			27,259
67,687	Sales of Sera, Vaccines, Vaccine Lymph, &c.		74,921
8,229	Rent		8,071
	Deficit transferred to Contingency Reserve after charging to Expenditure		
20,340	£10,001 for additions to property and equipment		11,097
£123,872			£121,348

Fund.

£		£
1,606	Interest on Investments (gross)	1,606
342	Balance Deducted from Fund	307
£1,948		£1,913

Studentship Fund.

£		£
290	Interest on Investments (gross)	290

Scholarship Fund.

£		£
217	Interest on Investments (gross)	217
128	Balance Deducted from Fund...	133
£345		£350

INVESTMENTS AT 31st DECEMBER 1953.

GENERAL FUND.

Nominal Value		Balance Sheet Value		Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	..	£74,800
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	..	37,496
£32,000	4 per cent. Funding Stock, 1960-90	25,995	..	32,480
£64,000	3½ per cent. War Stock, 1952, or after	63,408	..	54,240
£38,000	3 per cent. Savings Bonds 1955/65	35,000	..	34,125
£69,600	,, ,, ,, 1960/70	69,723	..	63,684
£38,300	,, ,, ,, 1965/75	33,857	..	34,276
£35,495	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	55,495	..	46,894
£20,000	,, ,, ,, ,, ,, 1967/72 ..	20,259	..	17,300
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	1,898	..	1,770
£15,000	,, ,, 3½ ,, ,, ,, 1976/79 ..	14,925	..	14,100
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	3,852
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65 ..	21,989	..	23,875
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	18,662
£2,900	Commonwealth of Australia 4½ per cent. Stock, 1960/62 ..	2,666	..	3,001
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74 ..	12,121	..	10,260
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75 ..	2,687	..	2,685
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	..	816
£4,000	Bankers Investment Trust Ltd., Deferred Stock	7,806	..	8,002
£3,250	Debenture & Capital Investment Trust Ltd., Ordinary Stock ..	6,586	..	7,313
£1,125	General Consolidated Investment Trust Ltd., Ordinary Stock ..	2,236	..	2,587
£3,750	London & Montrose Investment Trust Ltd., Ordinary Stock ..	7,893	..	9,750
£2,500	London Scottish American Trust Ltd., Deferred Stock ..	6,942	..	7,375
£1,500	London Trust Co., Ltd., Deferred Stock	3,229	..	3,780
£1,180	Lowland Investment Co Ltd., Ordinary Stock	2,683	..	2,578
£5,625	Mercantile Investment & General Trust Co. Ltd., Ordinary Stock	13,401	..	12,853
£5,000	Rio Claro Investment Trust Ltd., Ordinary Stock	11,192	..	10,875
£2,500	River Plate & General Trust Co., Ltd., Deferred Stock ..	7,691	..	7,313
£3,500	Sphere Investment Trust Ltd., Ordinary Shares	8,211	..	8,969
£1,350	Standard Trust Ltd., Ordinary Stock	2,723	..	3,255
£5,000	Sterling Trust Ltd., Ordinary Stock	8,731	..	10,775
£6,750	Third Guardian Trust Ltd., Ordinary Stock	8,663	..	8,808
£6,000	United States Debenture Corporation Ltd., Ordinary Stock .	12,553	..	13,110
£1,000	Witan Investment Co. Ltd., Ordinary Stock	11,145	..	9,220
		£620,917		£600,831

SINKING FUND FOR FREEHOLD BUILDINGS.

£4,500	3 per cent. Funding Stock, 1959-69	3,876	..	4,185
£10,200	4 ,, ,, ,, 1960-90	9,079	..	10,353
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	..	17,630
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	..	3,412
£6,700	,, ,, ,, 1960/70	6,454	..	6,131
£31,600	,, ,, ,, 1965/75	31,600	..	28,282
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	..	2,025
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	..	2,064
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	6,260	..	5,664
£3,000	,, ,, 3 ,, ,, ,, 1968/73 ..	2,916	..	2,685
£3,000	Third Guardian Trust Ltd., Ordinary Shares, 5/- paid	750	..	1,650
		£88,088		£84,081

PENSION FUND.

Nominal Value		Balance Sheet Value		Market Value
£22,000	4 per cent. Funding Stock, 1960-90	£17,165	..	£22,330
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173	..	15,480
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	..	2,018
£1,000	3 „ „ „ 1965/75	1,000	..	895
		£35,543		£40,718

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705	..	2,842
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986	..	1,678
£2,65[illegible]	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757	..	1,961
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097	..	943
		£8,545		£7,424

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, 3rd Issue	1,000	..	1,000
£500	3 per cent. Savings Bonds, 1960/70	500	..	457
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	..	3,741
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903	..	797
		£7,606		£5,995

RE-ENDOWMENT FUND.

£3,400	3 per cent. Savings Bonds, 1960/70	£4,941	..	£4,941

The Lister Institute
of
Preventive Medicine

Report of the Governing Body,

1954

Chelsea Bridge Road,
London, S.W. 1.

June 17th. 1954

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Superintendent of Elstree Laboratories: W. d'A. Maycock, M.B.E., M.D.

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A. Felix, D.Sc., F.R.S. (*Public Health Laboratory Service*).
I. N. Asheshov, M.D. (*Medical Research Council External Scientific Staff*).
Elizabeth Hall Asheshov, M.Sc. (*Medical Research Council External Scientific Staff*).
R. W. Nichol, B.Sc. (*Agricultural Research Council Student*).
F. Knight, B.Sc. (*Agricultural Research Council Student*).
S. Tuncman, M.D. (*Turkey*).

GUINNESS-LISTER RESEARCH UNIT

B. A. D. Stocker, M.D., M.R.C.S., L.R.C.P.
C. J. Perret, M.A.
C. Quadling, B.Sc.

BIOCHEMISTRY

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S. (*Professor of Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
*Marjorie G. Macfarlane, D.Sc., Ph.D.
*J. Baddiley, D.Sc., Ph.D.
R. A. Gibbons, B.Sc., Ph.D.
A. P. Mathias, B.Sc., Ph.D.
G. A. Jamieson, M Sc. (*Research Student*).
G. Owen, M.B., Ch.B., B.Sc. (*Research Student*).
M. Ruszkiewcz, M.Sc. (*Research Student*).
Marian Gibbons, B.Sc. (*Research Assistant*).
E. M. Thain, B.Sc., Ph.D., A.R.I.C. (*Imperial Chemical Industries Fellow*).
Winifred M. Watkins, B.Sc., Ph.D. (*Beit Memorial Research Fellow*).
J. G. Buchanan, M.A., Ph.D. (*Department of Scientific and Industrial Research Grantee*).
J. V. McLoughlin, M.Sc. (*Medical Research Council Grantee*).
C. J. M. Rondle, M.A. (*Medical Research Council Student*).
J. D. Feinberg, M.S., Dr. V. M. (*U.S.A.*).
K. Knox, M.Sc. (*Australia*).
J. O'Dea, B.Sc. (*Australia*).
L. Szabo, Dr. ès Sc. (*France*).
R. E. Handschumacher, Ph.D. (*U.S.A.*)
Dorothy J. Buchanan, Ph D. (*U.S.A.*)
R. Hodges, M.Sc. (*1851 Exhibitioner*).
Y. E. S. Gabr, B.Sc., Ph.D. (*Egyptian Government Student*).

BIOPHYSICS

†R. A. Kekwick, D.Sc., (*Reader in Chemical Biophysics in the University of London*).
§Margaret E. Mackay, M.Sc., Ph.D. (*Medical Research Council External Scientific Staff*).
B. Cinader, B.Sc., Ph.D., (*Agricultural Research Council*).
P. Wolf, M.B., Ch.B.
E. A. Caspary, B.Sc.
Professor N. H. Martin, M.A., B.M., B.Ch., B.Sc. (*Honorary Research Associate*).

NUTRITION

§Dame Harriette Chick, D.B.E., D.Sc.
§E. Margaret Hume, M.A.

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†Appointed Teacher of the University of London.
*Recognised Teacher of the University of London.
§Honorary Member of Institute Staff.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE)

B. G. F. Weitz, M.R.C.V.S.
J. Rodican, B.Sc.
Janet M. Bishop, B.Sc.

PREPARATION AND STUDY OF SMALLPOX VACCINE (ELSTREE)

*D. McClean, M.B., B.S., M.R.C.S.
L. H. Collier, M.D.
C. Kaplan, M.B., Ch.B., M.Sc.

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE)

*A. F. B. Standfast, M.A., Dip.Bact.
Dorothy H. Card, B.Sc.
‡K. B. Linton, B.Sc.
Doraine Thow, B.Sc.
Margaret E. Rowatt, B.Sc., Ph.D. (*Public Health Laboratory Service*).
Jean M. Horton, M.A., Ph.D.

BLOOD PRODUCTS (ELSTREE)

*W. d'A. Maycock, M.B.E., M.D.
‡L. Vallet, B.A.
Lisa L. Lam, M.Sc.
Jean Addey, B.Sc.
‡Shirley M. Evans, B.Sc.
‡Patricia Sherman, B.Sc.

BIOCHEMISTRY (ELSTREE)

*D. E. Dolby, B.Sc., Ph.D.

RESEARCH UNITS HOUSED AT THE INSTITUTE:—

MEDICAL RESEARCH COUNCIL

Blood Group Research Unit.

§R. R. Race, Ph.D., M.R.C.S., L.R.C.P., F.R.S.
Ruth Sanger, B.Sc., Ph.D.
Joan S. Snrath, B.Sc.

Blood Group Reference Laboratory.

§A. E. Mourant, M.A., D.Phil., D.M.
Dorothy M. Parkin, M.R.C.S., L.R.C.P.
Elizabeth W. Ikin, M.Sc.
Jean Graff, B.Sc.

ADMINISTRATION

Secretary and Accountant - - - S. A. White, A.A.C.C.A.

Elstree Secretary and Estate Manager - F. K. Fox.

Solicitors:
Field, Roscoe & Co.
52, Bedford Square, W.C.1.

Auditors:
Cooper Brothers & Co.,
14, George Street, Mansion House, E.C.4.

*Recognised Teacher of the University of London.
§Honorary Member of Institute Staff.
‡Working at Chelsea.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine,

June 17th. 1954

REPORT OF THE GOVERNING BODY

The Governing Body has the honour to present its report of the work of the Institute for the year 1953/54.

GOVERNING BODY

At its last meeting the Council re-elected Sir Henry Dale, Sir Paul Fildes and Sir Wilson Jameson as its representatives on the Governing Body until 31st December, 1954. In accordance with the Articles of Association Professor Morgan retired from the Governing Body and was succeeded by Dr. D. McClean as the Scientific Staff's representative.

The Governing Body has noted with pleasure the appointment of Dr. A. A. Miles to the rank of Commander of the Order of the British Empire and also the conferment on him of the title of Professor of Experimental Pathology.

COUNCIL

At last year's Annual General Meeting the three retiring members of the Council, The President of the Royal College of Surgeons, Professor H. B. Maitland and Professor Sir Rudolph Peters, were re-elected. During the year Sir Merrik Burrell was appointed by the Royal Agricultural Society as its representative in succession to the late Sir William Dampier.

The three members of the Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Professor Sir Alexander Fleming and Sir Henry Dale, each a representative of the Members of the Institute, and Professor Sir Howard Florey, the representative of the University of Oxford.

MEMBERS

The Governing Body records with regret the deaths during the year of Professor E. P. Cathcart, Dr. M. H. Gordon, Dr. T. W. Lumsden, Professor F. C. Minett and His Grace the Duke of Westminster.

STAFF

Sir Percival Hartley retired in October, 1953. As announced in last year's Annual Report Dr. B. A. D. Stocker was appointed head of the new Guinness-Lister Research Unit, which began work at the Institute on 1st October last. Mr. C. J. Perret and Mr. C. Quadling were appointed to the staff of this Unit.

The Governing Body takes pleasure in reporting that the University of London has appointed Dr. R. A. Kekwick a Teacher in Chemical Biophysics and that the Council of the Chemical Society has awarded Dr. J. Baddiley the Corday-Morgan Medal and Prize for the most meritorious contribution to experimental chemistry in 1952.

Mr. B. Weitz was appointed to take charge of the Serum Department in succession to Dr. W. d'A. Maycock who has now taken charge of the Blood Products Laboratory.

Mr. J. Rodican was appointed to the Serum Department, Dr. C. Kaplan to the Smallpox Vaccine Department, Miss D. Thow to the Bacterial Vaccines Department and Mrs. L. Lam (*nee* Lorenz) to the Blood Products Laboratory. Miss J. M. Bishop joined the Elstree staff to assist in the work undertaken on behalf of the Colonial Office. Mr. A. P. Mathias was given a temporary appointment in the Biochemistry Department and Mr. M. Ruszkiewicz was awarded an Institute studentship.

During the year Mr. M. J. Crumpton and Mr. A. P. MacLennan completed the tenure of their studentships and Miss K. Cook and Mr. J. D. Pearson resigned their posts.

Dr. A. Felix of the Public Health Laboratory Service and Dr. and Mrs. I. Asheshov, formerly of the New York Botanical Gardens, are now working at the Institute.

Professor Miles, at the invitation of the United States Army authorities lectured at the Army Medical Service Graduate School, Washington, in April. Professor Miles also attended a meeting of the expert committee on Biological Standardisation of the World Health Organisation in Geneva.

A meeting of the Organising Committee of the 5th International Congress on Blood Transfusion in Paris was attended by Dr. Maycock. Dr. McClean attended the Conference on Immunization at Frankfurt organised by the European Office of the World Health Organisation and at the invitation of the Colonial Office Mr. Weitz went to Malaya to attend a conference on the epidemiology of Yellow Fever.

The Blood Group Research Unit and the Blood Group Reference Laboratory of the Medical Research Council are still accommodated at the Institute.

The Governing Body notes with satisfaction the successful continuance of the researches under Professor Morgan and under Dr. Baddiley in his department; and under Professor Miles, all of which is made possible by the generous benefaction of the Nuffield Foundation.

MICROBIOLOGY

Hæmophilus pertussis antigens. Mr. A. F. B. Standfast and Dr. Jean Horton have continued their work on the chemical fractionation of *H. pertussis* to isolate the antigen inducing protection in mice. Antisera to ethanol precipitates of phenol extracts or of tryptic digests of the bacillus protect mice passively; and mice injected with the fraction from tryptic digests are actively immunized.

The relation of two antigens obtained from extracts of cells broken in the Hughes press—Pillemer's protective antigen and the hæmagglutinin, is being investigated.

The distinction of the agglutinogen and the protective antigen (1953 Report) has been further confirmed by adsorption experiments with purified agglutinogen and with bacilli that have lost their surface agglutinogen; agglutinin is not protective, and protective antibody does not agglutinate.

Dr. M. E. Rowatt has worked on the growth of *H. pertussis* in media containing blood. Freshly isolated strains will not grow on Cohen's medium solidified with agar even after extraction of the agar with methanol or pretreatment of the casamino acid with charcoal. They grow when blood, serum, or certain preparations of charcoal are added. Some preparations of albumin can replace serum. Organisms grown on blood Cohen agar are better than those grown on serum Cohen agar as an inoculum for liquid Cohen's medium. Growth in the liquid medium is improved by the addition of 1/1,000 blood; and lysed red cells promote growth more effectively than serum. The effect is not due to catalase.

The improvement in growth on blood media obtained by pretreating the casamino acid with charcoal proved not to be associated with removal of oleic acid, as measured by microbiological assay with a *Corynebacterium* species.

Mr. Standfast and Miss K. Cook, in conjunction with Dr. J. O. Irwin, of the London School of Hygiene and Tropical Medicine, continued their investigation on the mouse test for potency of Whooping Cough Vaccines for the Medical Research Council Whooping Cough Committee.

Vole bacillus. Miss D. H. Card has continued her investigation into the growth requirement of the murine strain of *Myco tuberculosis*.

Streptococcal Capsulation. Mr. A. P. MacLennan has concluded his work on streptococcal capsulation. A hyaluronidase was isolated from cultures of a capsulated, hyaluronic acid producing, group C streptococcus. Some capsulated group A strains produce a similar enzyme. The group C enzyme is rapidly destroyed at 37° in the absence of its substrate, hyaluronic acid. It is antigenic, giving rise to antibody which neutralizes the activity of the enzyme but which is inactive against other streptococcal hyaluronidases and against the testicular enzyme. The appearance of hyaluronic acid and capsules represents an excess of hyaluronic acid synthesis over destruction by the enzyme. There is no evidence that the formation of the enzyme depends on the presence of hyaluronidase-producing mutants.

Protozoology. Dr. M. Robertson has continued her study of *Trichomonas foetus* in cattle in collaboration with Dr. W. R. Kerr (Department of Veterinary Research, Ministry of Agriculture, Northern Ireland). The duration of the "immunological paralysis," induced in calves under three weeks old by the injection of large doses of *T. foetus* antigen (Report 1953) is being measured in the now mature animals.

Dr. Robertson is investigating the antigens of the two serological varieties of *T. foetus* by means of the gel diffusion method of Ouchterlony. This method is also being used to study the inter-relations of different strains of *Tetrahymena* species which have been cultivated in bacteria free media.

Mr. R. W. Nichol has studied the life cycle of *Copromonas subtilus*, a colourless, euglenoid, flagellate from the fæces of toads. *Copromonas* has been isolated, and maintained in continuous culture with two bacterial species. Syngamy has been observed, and the process followed to the first division of the resulting zygote, thus confirming the early work of Dobell (1908).

Mr. D. Knight has worked on ciliates of the *Tetrahymena* group and on *Stylonichia* species.

Dr. J. G. Feinberg has prepared about 100 g. of freeze-dried *Trichomonas vaginalis* organisms. A part of this material has been extracted successfully with diethyleneglycol and ethyleneglycol and specific substances of high serological activity recovered. The materials have not yet been characterised chemically. Phenol-water extraction of the whole culture has yielded serologically specific protein fractions and a serologically inactive nucleic acid. The culture characteristics of *T. vaginalis* in various media have been studied and a new morphological character of the anterior flagella reported.

L-forms of Bacteria. Dr. Klieneberger-Nobel assisted by Dr. S. Tunoman, has studied a number of L-phase strains isolated from *Fusiformis*, *Proteus*, *Salmonella* and *Streptobacillus* species, with special reference to their filterability, their antigenic relationship to the bacterial phase, the conditions governing their reversion to the bacterial phase, and their general relationship to pleuro-pneumonia-like organisms. In collaboration with Mr. F. W. Cuckow of the Chester Beatty Institute, she has begun a morphological investigation of the filterable phase of organisms of the pleuropneumonia group and of L-forms of bacteria, by electron microscopy.

Bacterial Genetics. Dr. B. A. D. Stocker, assisted by Mr. C. Quadling, has continued his investigation of the genetics of the *Salmonella* group. Testing the interactions of different non-flagellated strains to produce flagellated forms has proved the existence of several further "Fla" genes, regulating the presence or absence of flagella. Three of these newly discovered "Fla" genes prove to be linked to a gene regulating the antigenic specificity of the phase 1 flagellar antigen. Testing the interactions of some of these strains, interpreted on a hypothesis of linear gene arrangement, has permitted mapping of the linear order of three different "Fla" genes and of the antigen-determining gene; and has made possible the first experimental test of the hypothesis that the *Salmonella* genes which can be transferred from cell to cell by phage particles are arranged linearly. Other work in progress includes experiments on the isolation by micro-manipulation of individual cells made motile by transduction, the transduction of resistance to streptomycin and to sodium azide, and the examination of new *Salmonella* phages for use in transduction experiments. Genetically "tagged" variants of a strain of *S. paratyphi B* have been prepared by transduction. In collaboration with Dr. G. G. Meynell, of the London School of Hygiene, these are being used in experiments on virulence in mice.

Bacterial Chemistry. Mr. J. Perret has been occupied in modifications of his "Constant Population Density" apparatus, and other apparatus required for researches on adaptive enzyme formation.

Vaccinia Virus. Dr. D. McClean, Mr. L. Vallet and Dr. L. H. Collier have continued their investigation of the antigenicity of vaccinia inactivated by ultra-violet light. The possibility existed that the immunity produced in rabbits might be due to traces of living virus. The maximum amount of living virus likely to have escaped detection by the sampling method used was determined statistically; rabbits inoculated with 5-10 times this amount of live virus suspended in serum or broth, failed to make a definite immune response. When, however, similar small doses of living virus were given with suspensions of over-irradiated virus, powdered glass, or killed *Chromobacterium prodigiosum*, there was a definite increase in circulating antibody and a modification of the response to subsequent vaccination in the majority of rabbits. The

dose of living virus, was, however, much greater than could have escaped detection in the irradiated vaccines which regularly produced immunity in the previous experiments. An attempt is now being made to determine the smallest dose of living virus which will provoke significant antibody formation when given with large particulate matter.

Dr. L. H. Collier has concluded his study of methods of preserving vaccinia virus. A vaccine consisting of partially purified virus freeze-dried in 5% peptone is satisfactorily stable on storage, conforming with the standard of potency required by the Therapeutic Substances Regulations after incubation for at least one month at 37°C, whereas glycerinated lymph becomes useless within a few days at this temperature. This vaccine has been tried extensively by the three Services of the armed forces with satisfactory results. A technique of large scale manufacture has been devised. The dried vaccine will be available for use in hot climates and will partially replace the glycerinated lymph held as epidemic reserves in this country.

Dr. Collier is continuing his work on auto-interference by vaccinia virus. When mixtures of heat inactivated and fresh vaccinia are injected intracutaneously in rabbits, the dead virus interferes with proliferation of the living vaccinia. The histology of the skin reactions is being investigated in collaboration with Dr. Janet Niven of the National Institute for Medical Research.

In collaboration with Dr. J. O. Irwin of the Medical Research Council Statistical Unit, Dr. Collier has completed a study of the accuracy of the pock counting method for titrating vaccinia virus in embryonated eggs, and of the relation between dilution of virus suspension and number of pocks produced on the chorioallantois.

Bacterial Viruses. Dr. D. E. Dolby has continued his study of substances inhibiting the multiplication of the T series of bacteriophages in *Bact. coli B.* The inhibition of phage multiplication by borate differs from that of arsenite and cyanide, and depends on the oxidation-reduction potential of the medium. In addition, arsenite affects a late phase in the reproduction of the virus, inhibiting phage-production even when added shortly before the bacteria begin to burst.

PATHOLOGY

Plasma Substitutes. Dr. W. d'A. Maycock and Mrs. L. L. Lam have investigated the mechanism of the prolonged urinary excretion of intravenously injected dextran, in rabbits and mice, after dextran is no longer detectable serologically in the serum, and the uptake of intravenously injected dextran by, and its rate of disappearance from, certain tissues, particularly the liver.

Pharmacology of Serum fractions. Professor A. A. Miles, Dr. D. L. Wilhelm, Dr. M. Schachter and Dr. M. E. Mackay have investigated large-molecular substances present in normal guinea-pig serum, that have biological effects in the guinea-pig. Simple dilution of guinea-pig plasma or serum activates substances that increase the permeability of the capillaries and fix histamine so as to modify its action on the isolated guinea-pig intestine. The serum also contains an inhibitor of the permeability effect. Ether and electrophoretic fractionation of the serum yields lipoprotein alpha globulins that increase capillary permeability and produce a typical hypotensive effect in the whole animal, and fix histamine. The permeability factors produced by dilution and by fractionation, and the hypotensive factor, are antagonized by soya bean inhibitor, and by a natural inhibitor present in an alpha-globulin associated with the albumin fraction; and on other grounds appear to be identical. The identity of these factors with fibrinolysin cannot yet be established. The histamine-fixing substances appear to be distinct.

The role of these substances in mediating the vascular phenomenon of inflammation and shock is under study; they are not histamine-liberators.

The investigation has been extended to similar substances in other mammalian sera, tested in the rat, guinea-pig, rabbit, cat and dog. The species inter-actions of the biologically active proteins in these sera are complex and diverse. Dilution activates histamine-fixing substances in many sera. Permeability factors are present without activation in most sera, though those of man and rat contain a dilution-activable permeability factor as well.

Experimental Pathology. Dr. Wilhelm and Professor Miles are studying the changes in capillary endothelium and endothelial cement substance induced by agents that increase capillary permeability. Dr. Wilhelm has investigated the regeneration of tracheal epithelium in rats deficient in Vitamin A, and, in collaboration with Professor G. R. Cameron, F.R.S., of University College Hospital Medical School, has studied the vascular pattern of scar tissue in rat skin.

Venoms. In collaboration with Dr. Thain, Dr. Schachter has studied an unidentified smooth muscle stimulant in wasp venom. Analysis of preparations, including some purified by chromatography, indicates that the stimulant is probably a peptide and that its various pharmacological properties are due to a single substance. Its chemical composition is under investigation.

IMMUNOLOGY

Antitoxins. Dr. Dolby has begun a survey of methods for removing the inactive polypeptides which are produced during the pepsin treatment of antitoxins and which contaminate the final product. Salt precipation methods have not proved satisfactory, but some improvement can be obtained by low-temperature alcohol fractionation. Adsorption methods are now under investigation.

He has also continued his study of the kinetics of pepsin activity, particularly fractions that are optimally active at pH 2 and 3·25.

Toxin-Antitoxin Reactions. Studies on the intereaction of *Cl. welchii* antitoxin and *Cl. welchii* lecithinase have been continued by Dr. Cinader. The Ehrlich Phenomenon has been analysed in the terms of this system and has proved to be due to an expression of the shape of the neutralization curve.

Simultaneous addition of substrate and antitoxin to toxin has been studied in systems having the same relative but different absolute concentrations. In regions of high antigen excess the equilibrium depends much less on the absolute concentrations than it does near the neutral point. The absorption of enzyme and antibody by enzyme-antibody floccules has been studied.

An apparatus has been constructed for electrophoresis of antigens and antibodies in agar for subsequent serological analysis by the gel diffusion method. Electrophoretic components have been localized in the agar strip by making imprints on filter paper, staining and scanning. By using this technique, three electrophoretic components with antibody activity were demonstrated in *Cl. welchii* horse antisera.

In collaboration with Mr. B. Weitz, the method is being applied to the inter-action of horse antigen and its corresponding rabbit antibody.

Identification of Insect Blood Meals. Mr. Weitz and Miss J. M. Bishop have continued the research on suitable methods for the identification of sera of closely related mammalian species.

The inhibition of agglutination by antisera, of red blood cells coated with the corresponding serum proteins after treatment with tannic acid, has proved to be highly specific and of sufficient sensitivity for application in identity tests of sera ingested by blood sucking insects. The specificity is such that the sera of closely related species such as warthog, bushpig and domestic pig, and of man and several species of monkeys, can be readily distinguished.

Investigation with feeds from *Glossina* fed on various known species of animal proved that the technique could be used without significant loss of specificity even after partial digestion of blood meals.

The application of these techniques to mosquitoes is being investigated, particularly in relation to possible vectors of virus disease, as a help to establish the main reservoir hosts concerned.

BIOCHEMISTRY

The human blood group substances. Professor W. T. J. Morgan and Dr. W. M. Watkins have studied the action of a partially purified enzyme preparation obtained from *Trichomonas fœtus* on certain of the specific blood group receptors on the erythrocyte surface. The *T. fœtus* enzyme inactivates the H specific structures and those responsible for M and N specificity but is without action on the A, B, P or S receptors. Treatment of *Rhesus* (D) positive cells with the *T. fœtus* enzyme leads to the development of specific agglutinability in saline with incomplete anti-D serum. The enzymes responsible for the inactivation of the H and M receptors can be differentiated by inhibition tests. The destruction of the H character is inhibited by L-fucose and D-galactosamine whereas these sugars do not inhibit the inactivation of the M receptors.

Erythrocytes which have had their H-receptors destroyed by the *T. fœtus* enzyme are no longer agglutinated by the PRB strain of influenza virus. The treatment of red cells with the same virus does not bring about the destruction of the H-specific structures.

A potent human O cell agglutinin with H-specific character has been examined. The behaviour of this agglutinin with authentic A_1A_1 and A_1O red cells confirms the belief that anti-H agglutinins do not detect a product of Bernstein's *O* gene and that within the ABO system the homozygous (AA, BB) or heterozygous (AO, BO) nature of the cells cannot be determined by anti-H reagents.

Dr. Watkins has examined methods for the purification of the enzymes obtained from *Trichomonas fœtus* which destroy the serological activity of the human blood group substances. Purification of the enzyme preparation has been achieved by fractionation at 0° with ammonium sulphate and by fractionation at −5° with ethanol. Further work is in progress to determine the chemical changes associated with the enzymic degradation of the blood group substances.

Mr. Knox and Professor Morgan have investigated the effect of weakly alkaline (pH 8·4) conditions on the blood group substances. It is known that they lose their serological activity on heating at this pH and that this change is associated with a decrease in viscosity and the formation from the N-acetylhexosamine components of a chromogen which gives a colour with Ehrlich's reagent. Heating in alkali appears to bring about a general depolymerisation to yield a series of dialysable fragments and the material which is precipitated by 60% ethanol from these diffusible substances has weak serological activity. When the heating is not too prolonged the indiffusible part of the blood group substances does not differ significantly in chemical composition from the untreated preparation. After mild alkaline treatment of the group substances with barium carbonate, a series of at least four chromogen-containing oligosaccharides have been detected in the diffusate and attempts are now being made to separate these oligosaccharides and identify their component sugars.

Mr. C. J. M. Rondle has continued to study the oxidation of blood group mucoids by hypoiodous acid. The amount of free reducing group found in these substances has been much greater than might have been expected from the particle weight, and the presence of at least forty carbohydrate chains in the intact molecule is indicated.

A number of serologically active mucoid materials have been analysed before and after oxidation and ion-exchange chromatography has been used to obtain individual assessments on the oxidised materials of the proportion of N-acetyl glucosamine and N-acetyl galactosamine present. There is no association between hexosamine ratio and immunological activity; and the serological properties of the blood group mucoids do not change significantly after oxidation with hypoiodous acid.

Dr. R. A. Gibbons, Mrs. M. N. Gibbons and Professor Morgan have isolated and purified the blood group substances from a number of ovarian cyst fluids derived from individuals belonging to blood groups A_1, A_2, B, A_1B, and O. Fourteen materials, all of which are essentially homogeneous, have been briefly analysed chemically and compared, and their behaviour towards mild acid hydrolysis has been briefly examined.

Mrs. M. N. Gibbons has started work on the quantitative precipitin technique for the determination of the purity of the blood group substances. She has also investigated Somogyi's reagents of varying alkalinity for the determination of reducing sugars, and colorimetric reagents, including catechol, amino-guanidine, and anthrone, for the determination of sugars in strongly acid solutions. Of the colorimetric reagents investigated only anthrone holds promise of being useful for the quantitative estimation of galactose in blood group substances.

Mr. O'Dea has completed his studies on the liberation of formaldehyde from carbohydrates during oxidation with periodate. Small amounts of disaccharides and a number of polysaccharides, including glycogens and dextrans, have been oxidised and the formaldehyde determined by the method described in last year's report. Examination of the disaccharide maltose and the polyfuranoside galactocarolose has shown that certain structures, which arise in many oxidations, combine with formaldehyde and give a reduced yield of this substance. The inclusion of small amounts of p-hydroxybenzaldehyde in oxidation mixtures prevents the combination of the liberated formaldehyde with the active structure in the oxidised sugar.

By varying the conditions of oxidation, a selective method has been developed for the estimation of the non-reducing end-group in polyfuranosides, and applied to the estimation of furanose ringform in monosaccharide solutions.

Dr. G. Owen has isolated blood group substances from meconium and compared their properties with those materials isolated from ovarian cyst fluids. The wall of the alimentary tract has been examined for its content of group substance in an attempt to account for the large amount of blood group substance in the meconium. Dr. Owen's work on the nature and immunochemistry of the "Lewis" group substances has been stopped owing to the lack of potent "Lewis" Le^a and Le^b blood grouping sera.

Toxins and Enzymes. Dr. M. G. Macfarlane has continued her studies on the osmotic properties of kidney mitochondria; these particles when respiring, like liver mitochondria, can maintain an internal concentration of ions higher than that of the medium but are less stable on isolation than liver mitochondria. Dr. Macfarlane is also continuing studies on the mechanism of action of *Cl. welchii* lecithinases and other lecithinases on tissue components.

Methods for purifying *Cl. welchii* lecithinase, for use in this work, have been explored with the assistance of Miss N. Czeczowiczka. After preliminary concentration of the crude toxin with ammonium sulphate, and fractionation with acetone in presence of calcium salts, which removes much of the pigment, the lecithinase can be co-precipitated with lecithin in presence of acetone, and recovered in fair yield, with considerable separation from other antigens present. Almost colourless products, containing up to 18,000 LD_{50} per mg. N have been obtained but complete separation from other antigens has not been achieved.

Bacterial Antigens. Professor Morgan and Dr. D. A. L. Davies (now of Microbiological Research Department, Porton) have completed and published their work on the O somatic antigen of *Shigella dysenteriæ* (Shiga) Antigenic material, which separated on centrifugation between 25,000 and 100,000 g., contained 4·5% N and 0·83% P and was free from detectable impurities as shown by fractional solubility tests, electrophoretic examination and behaviour in the ultracentrifuge. The antigen has a particle weight of the order 10^7. An uncombined, undegraded specific polysaccharide was recovered from the bacterial extracts; the substance was not deposited from aqueous solution after prolonged centrifugation at 100,000 g. Professor Morgan is now studying a lipopolysaccharide which can be dissociated from the whole antigen and which is an extremely powerful pyrogen. Intravenous injection into rabbits of 0·001 ug. brings about a rise in body temperature of 0·6° and induces the formation of high titre Forssman heterophile antibodies.

Coenzyme A. Drs. J. Baddiley, J. G. Buchanan and E. M. Thain have continued their efforts to synthesise coenzyme A. Several routes, based upon known methods for pyrophosphate synthesis, have been explored without success. The cause of these failures is uncertain but a thorough investigation on model substances is in progress. In this way it is hoped that the interfering groups in the intermediates will be recognised and then modified accordingly.

Dr. Baddiley and Dr. A. P. Mathias have confirmed that pantothenyl cysteine is a precursor of CoA in *Acetobacter suboxydans*. The 4'-phosphate of this substance has been synthesised. This is active as a CoA precursor but less so than the unphosphorylated peptide. The significance of this finding is being examined by Drs. D. E. Hughes and W. S. Pierpoint of Sheffield University. Also in collaboration with these workers, Drs. Baddiley and Mathias have found that cysteine-deficient cells of *Lactobacillus arabinosus* will phosphorylate pantothenic acid, giving the 4'- phosphate. However, this is not used by this and other microorganisms as a CoA precursor when supplied in the medium.

Cytidine Nucleotides. An investigation of the nucleotides in *Lactobacillus arabinosus* has been made by Dr. Baddiley and Dr. Mathias. Dried cells of this organism were examined by paper chromatography and ion-exchange methods. The nucleotide fraction was composed largely of the 5'- phosphates of adenosine, uridine and cytidine. Cytidine-5' phosphate has not previously been found in nature, except as a structural unit in ribonucleic acid. When fresh, rapidly growing organisms were extracted with boiling aqueous alcohol no cytidine-5' phosphate was found, but the following nucleotides were present: diphosphopyridine-nucleotide, adenosine-5' phosphate, uridine-5' phosphate, adenosine-diphosphate, uridine-diphosphate,. Several other phosphates of uridine, adenosine and guanosine were tentatively identified. Two cytidine nucleotides (CPX and CPY) were present. These were very similar in their properties and have been shown to be derivatives of cytidine—5' phosphate in which a group (X and Y respectively) is joined in ester linkage with the phosphate residue. These substances are being investigated in more detail.

Riboflavin Precursors. The course of riboflavin synthesis in *Eremothecium ashbyii* is being studied by Dr. Baddiley, Dr. Buchanan and Dr. R. E. Handschumacher and Mr. R. Hodges. This mould normally produces large amounts of riboflavin but a mutant has been obtained which forms only small amounts of the vitamin. It is hoped that riboflavin precursors will accumulate in the mutant and that these may be identified. Experiments are in progress in which suspected intermediates labelled with C^{14} are supplied in the medium. Methods have been developed for the location of isotope in the riboflavin formed.

The chemical synthesis of certain purine nucleoside precursors is being attempted. It is believed that some of these precursors may be common to both purine nucleoside and riboflavin formation in the mould.

Active Methionine. Dr. Baddiley and Mr. G. A. Jamieson, in collaboration with Dr. G. L. Cantoni, of Western Reserve University, Cleveland, have fully substantiated the proposed formula for active methionine. The presence of a sulphonium group was established by electrophoresis and its position with respect to the adenosine residue confirmed by hydrolysis of active methionine to "adenine thiomethyl pentoside." Dr. Baddiley and Mr. Jamieson have synthesised S-(5'-deoxyadenosine-5')-methionine (active methionine) from "adenine thiomethyl pentoside" and 2-amino-4-bromobutyric acid. This is indistinguishable from the natural substance for the enzymic methylation of nicotinamide and for choline synthesis.

Cyclic Phosphates. The steric factors governing phosphate group migration and cyclic phosphate formation in sugars have been studied by Dr. Baddiley, Dr. Buchanan and Dr. L. Szabo. It has been observed that glucosides readily yield 4 : 6-cyclic phosphates and attempts are being made to correlate this finding with the acid-catalysed migration of phosphate groups from position-6 in certain sugars.

Bacterial Decomposition of Thioethers. Dr. Baddiley and Dr. Handschumacher have observed that an as yet unidentified bacterium hydrolyses thioethers (adenine thiomethyl pentoside and methionine) to mercaptans and hydroxy compounds. The nature of this unique reaction is under investigation.

BIOPHYSICS

Diffusion, Ultracentrifuge and Electrophoresis Studies. Dr. R. A. Kekwick in collaboration with Dr. J. A. Bonnell (M.R.C. Unit for Research in Industrial Medicine, London Hospital, E. 1) has studied the serum and urinary proteins from a series of cases of cadmium poisoning. The urinary proteins appear to be of much lower molecular weight than any of the serum proteins, which have normal electrophoretic characters.

Mr. E. A. Caspary has continued the physico-chemical study of purified human fibrinogen. It has been established that the molecular weight of human fibrinogen is 341,000 $\pm$ 10 000. In solutions containing 0·15 g. protein/100 ml. or less, the molecule disassociates into units of the order of 100,000 molecular weight.

Acetylation of fibrinogen with 2' acetyl thioethylacetamide has shown that the reactivity towards thrombin changes with the degree of acetylation. The electrophoretic mobility of acetylated fibrinogen is higher at alkaline pH values than that of the untreated material.

Human Plasma and Plasma Products. During the past year, the Blood Products Laboratory has continued to prepare freeze-dried human plasma, plasma fractions and derivatives for the Ministry of Health.

Equipment. In collaboration with the A.P.V. Company Ltd., Wandsworth Park, London, S.W. 18, Dr. R. A. Kekwick and Mr. L. Vallet have designed a vessel for the large scale aseptic fractionation of human plasma proteins. The operational characteristics of the vessel, which has a capacity of 80 l, have been studied. The vessel is in use for the large scale production of gamma globulin.

Mr. L. Vallet has been engaged in work connected with the design and installation of equipment in the new laboratory at Elstree.

Animal Sera. Dr. M. E. Mackay has applied the method devised for the fractionation of human plasma with ether to serum from a number of animals other than man.

By slight modifications in the technique, fractions containing gamma globulins and albumins have been obtained from guinea-pig, rat, rabbit, dog, cat, horse, sheep and bovine sera. The purity of the fractions varied from animal to animal, but in some cases by a further step it was possible to obtain material having only one electrophoretic component.

In collaboration with Professor Miles, Dr. Schachter and Dr. Wilhelm, alpha and beta lipoprotein globulins have also been prepared, and examined for specific biological activity. An investigation of the properties of an alpha globulin associated in the fractionation with albumin has been started. There is some evidence that enzyme inhibitors are present in this fraction.

BLOOD

Blood Group Research Unit. The Blood Group Research Unit has continued its search for "new" blood group antibodies and the genetical investigation of the antigens they define. Much of the Unit's time in the last year has been given to the elucidation of a new Rh antigen, f, present in the blood of two-thirds of white people. The antibody which revealed the new antigen was found in the serum of a hæmophiliac who had suffered a reaction to transfusion, which was sent by Dr. P. Vogel and Dr. R. E. Rosenfield of New York.

Other work included a continuation of the blood grouping of families for evidence of genetic linkage between the blood group genes themselves and between the blood group genes and certain disease genes. The Unit is collaborating with Dr. Sheila Callender of the Nuffield Department of Clinical Medicine, Oxford, in a genetical and hæmatological study of pernicious anæmia; and with Dr. Eliot Slater and Mr. J. Shields of the Maudsley Hospital, in the investigations of twins.

With the Blood Transfusion Service, Sheffield, the Unit investigated a curious case of mixed blood in a donor who, when *in utero*, had undoubtedly received a primordial red cell graft from her twin brother.

The Unit is greatly indebted to the Blood Group Reference Laboratory for a most generous supply of antisera; to Professor Sir Ronald Fisher, F.R.S., for continued help and encouragement.

Blood Group Reference Laboratory. The Laboratory has continued to supply blood grouping sera in increasing quantity and variety to users in Great Britain and abroad. In collaboration with the Department of Biological Standards of the National Institute for Medical Research and the Blood Products Laboratory, standard preparations of anti-D sera for National and International use have been made.

Further various rare hæmagglutinating antisera have been identified. In conjunction with Dr. H. Lehmann, of St. Bartholomew's Hospital, a hæmagglutinating antiserum has been prepared in rabbits which reacts specifically with human red cells containing fœtal hæmoglobin.

Anthropological blood group studies have been carried out in the field by Miss E. W. Ikin on Andaman Islanders and Arabs, and in the laboratory on Greeks, Touaregs, Abyssinians, Australian Aborigines and tribesmen from Uganda and Kenya.

Dr. D. M. Parkin has continued to study familial blood group antigens and the blood group aspect of skin grafting.

A further course of practical instruction in advanced blood grouping techniques, and of lectures on blood groups and transfusion was given to a number of pathologists concerned with blood transfusion, from Great Britain and abroad. Many laboratories abroad have been helped in setting up their own testing services, not only by the supply of testing sera but by the detailed testing of the red cells of their staff members.

The Governing Body again expresses its satisfaction with the high quality of the work of all members of the Staff which maintains and even increases the wide repute of the Institute.

As in the report for last year, however, they must note that this scientific success continues to develop an unbalance between expenses and revenue. The original endowments no longer suffice to maintain modern developments of research at modern prices. The Governing Body has the matter fully in mind and is exploring methods by which the position might be rectified.

PAUL FILDES,

Acting Chairman of the Governing Body.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1954

FINANCIAL REPORT OF THE GOVERNING BODY

1. The Balance Sheet for the year ended 31st December 1954 shows balances to the credit of the various funds as follows: Capital Fund £699,595; Specific Funds £135,124; Bequest Funds £18,667 and Contingency Reserve £44,035.

2. The General Fund Income and Expenditure Account shows the income for the year as £123,997 compared with £110,251 in 1953. Expenditure amounted to £124,678 against £121,348 last year. The deficit for the year is £681 compared with a deficit of £11,097 in 1953.

3. The year's deficit of £681 shown by the General Fund Income and Expenditure account has been written off against the Contingency Reserve.

4. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £8,019, £3,372 and £5,096 respectively.

5. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

19th May, 1955.

BALANCE SHEET

(1953) £		£	£	£
	Capital Fund:—			
	Donations, &c., received to date from the following:—			
2,000	Dr. Ludwig Mond (1893)		2,000	
46,380	Berridge Trustees (1893/98)		46,380	
10,000	Worshipful Company of Grocers' (1894)		10,000	
250,000	Lord Iveagh (1900)		250,000	
18,904	Lord Lister's Bequest (1913/23)		18,904	
7,114	William Henry Clarke Bequest (1923/6)		7,114	
3,400	Rockefeller Foundation (1935/6)		3,400	
500	James Henry Stephens Bequest (per Lloyds Bank Limited) (1938)		500	
22,035	Other Donations and Legacies (1891-1954)		22,169	
	General Fund Income and Expenditure Account Accumulated Surplus as at 31st December, 1953	339,333		
	Less Amount written off and loss on sale of investments	205		
339,333			339,128	
699,666				699,595
	Specific Funds:—			
90,555	Sinking Fund for Freehold Buildings	93,990		
36,108	Pension Fund	36,114		
5,020	Re-endowment Fund	5,020		
			135,124	
	Bequest Funds:—			
10,290	Jenner Memorial Studentship Fund	10,529		
7,925	Morna Macleod Scholarship Fund	8,138	18,667	
149,898				153,791
	Specific Grants and Legacies Unexpended:—			
772	Cancer Research Legacies (1937-50)		772	
2,492	Royal Society Grant (1951)		2,048	
3,806	Nuffield Foundation Grants (1952-4)		4,393	
111	Guinness Lister Research Grant (1953-4)		2,000	
7,181				9,213
	Contingency Reserve:—			
	As at 31st December 1953		44,716	
	Less Deficit on General Fund Income and Expenditure Account, 1954		681	
44,716				44,035
	Current Liabilities:—			
11,697	Creditors and accrued charges			15,721
£913,158				£922,355

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

REPORT OF THE AUDITORS

We have examined the above Balance Sheet and annexed Income and Expenditure Account which are in all the information and explanations which we considered necessary for our audit. In our opinion these accounts information required by the Companies Act, 1948, and show a true and fair view of the state of the Institute's

London, 20th May, 1955.

31st DECEMBER 1954.

(1953) £		£	£	£
	Fixed Assets :—			
	FREEHOLD PROPERTY at cost :			
73,548	Land and Buildings, Chelsea	73,548		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,053	
	(*Note*: *Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS :—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,525	(*Note*: *Additions and replacements since 31st December, 1920 have been charged to Revenue*)			98,525
	General, Specific and Bequest Funds.			
	Quoted Investments at cost, less amounts written off and Uninvested Cash :—			
		Investments	Cash	
620,917	GENERAL	607,532	—	607,532
	SPECIFIC :			
90,555	Sinking Fund for Freehold Buildings ..	93,507	483	93,990
36,108	Pension Fund	35,543	571	36,114
5,020	Re-endowment Fund	4,941	79	5,020
	BEQUEST :			
10,290	Jenner Memorial Studentship Fund ..	8,545	1,984	10,529
7,925	Morna Macleod Scholarship Fund ..	7,606	532	8,138
770,815		757,674	3,649	761,323	761,323
	(*Market Value £821,091*)			
	Current Assets :—			
31,385	Debtors and Payments in advance		57,360	
4,148	Bills Receivable		2,187	
8,285	Balance at Bankers and Cash in hand		2,960	
43,818				62,507
	(*Notes*: *See paragraph 4 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts.*			
	There is an outstanding capital expenditure commitment of £4,607 in respect of cottages at Elstree).			
£913,158				£922,355

TO THE MEMBERS.

agreement with the books of account. In our opinion proper books of account have been kept. We have obtained amplified by the information given in paragraph 4 of the Financial Report of the Governing Body give the affairs at 31st December, 1954, and of the deficit for the year ended on that date.

COOPER BROTHERS & CO.
Chartered Accountants

INCOME AND EXPENDITURE ACCOUNTS

GENERAL

(1953)		*Total Expenditure*	*External Contributions*	
£		£	£	£
51,122	Salaries and Wages	88,514	36,021	52,493
5,478	Emoluments of two members of the Governing Body in an Executive Capacity	5,632	—	5,632
1,822	Premiums on Federated Superannuation Policies	3,024	1,051	1,973
3,361	Premium on Group Pension Policy	3,259	155	3,104
2,634	Rent, Rates and Insurance	3,288	—	3,288
7,787	Gas, Water, Fuel and Electricity	10,774	2,223	8,551
1,486	Office Expenses, Stationery and Printing ...	1,483	172	1,311
815	Auditors' Fee	263	—	263
875	Travelling Expenses	715	63	652
1,739	Biochemistry Expenses	2,067	781	1,286
913	Microbiology, Immunology and Experimental Pathology Expenses	2,788	1,684	1,104
680	Biophysics Expenses	1,692	1,191	501
13,431	Serum, Vaccine and Vaccine Lymph Expenses	12,410	2,060	10,350
6,731	Animals	8,282	1 369	6,913
7,396	Animal House Expenses and Forage	8,069	665	7,404
9,139	Buildings, Alterations, Repairs and Renewals ...	13,720	406	13,314
1,218	General Apparatus and New Installations ...	628	209	419
789	Library Expenses	903	—	903
749	General Stores	1,083	—	1,083
473	Staff Canteen Loss	902	203	699
—	Blood Products Laboratory Expenses	4,870	4,870	—
3,260	Amount transferred to Sinking Fund for Freehold Buildings (including £8,011 Interest on Investments)	3,435	—	3,435
£121,348		£177,801	£53,123	£124,678

PENSION FUND.

£		£	£		£
1,913	Pensions	1,600	1,606	Interest on Investments (gross) ...	1,606
	Balance added to Fund ...	6	307	Balance deducted from Fund ...	—
£1,913		£1,606	£1,913		£1,606

JENNER MEMORIAL STUDENTSHIP FUND.

£		£	£		£
—	Stipend of Student	51	290	Interest on Investments (gross) ...	290
290	Balance added to Fund	239			
£290		£290	£290		£290

MORNA MACLEOD SCHOLARSHIP FUND.

£		£	£		£
350	Stipend of Student	89	217	Interest on Investments (gross) ...	227
—	Balance added to Fund	213	—	Post-War Credits	75
			133	Balance deducted from Fund ...	—
£350		£302	£350		£302

Fund.

(1953) £		£	£
	Interest and Dividends on Investments:		
24,423	General Fund	25,940	
2,836	Sinking Fund	3,011	
			28,951
74,921	Sales of Sera, Vaccines, Vaccine Lymph, &c.		86,404
8,071	Rent		8,642
11,097	Deficit transferred to Contingency Reserve after charging to Expenditure £10,001 for additions to property and equipment		681
£121,348			£124,678

Guinness - Lister Research Grant.

(1953) £		£	(1953) £		£
1,669	Salaries and Wages	5,291	—	Balance at 1st January, 1954...	111
4,447	Laboratory Expenses	2,820	7,500	Amount received	10,000
1,273	Alterations to Laboratories ...	—			
111	Balance carried forward ...	2,000			
£7,500		£10,111	£7,500		£10,111

Nuffield Foundation Grants.

(1953) £		£	(1953) £		£
5,270	Salaries, Wages, Laboratory Expenses and Animals	6,413	2,076	Balance at 1st January, 1954...	3,806
3,806	Balance carried forward ...	4,393	7,000	Amounts received	7,000
£9,076		£10,806	£9,076		£10,806

INVESTMENTS AT 31st DECEMBER 1954.

GENERAL FUND.

Nominal Value		Balance Sheet Value		Market Value
£80,000	4 per cent. Consolidated Stock, 1957	£74,273	..	£77,200
£43,600	3½ per cent. Conversion Stock, 1961, or after	43,514	..	38,586
£32,000	4 per cent. Funding Stock, 1960-90	25,995	..	32,960
£64,000	3½ per cent. War Stock, 1952, or after	63,408	..	55,840
£25,000	3 per cent. Savings Bonds 1955/65	25,000	..	25,000
£66,300	,, ,, ,, 1960/70	66,417	..	63,648
£38,300	,, ,, ,, 1965/75	33,857	..	36,002
£55,495	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	55,495	..	48,559
£20,000	,, ,, ,, ,, ,, 1967/72 ..	20,259	..	18,300
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	1,898	..	1,870
£15,000	,, ,, 3½ ,, ,, ,, 1976/79 ..	14,925	..	14,775
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	3,942
£25,000	New Zealand Government 3½ per cent. Stock, 1962/65 ..	21,989	..	24,375
£26,100	S. Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	19,444
£2,900	Commonwealth of Australia 4½ per cent. Stock, 1960/62 ..	2,666	..	3,045
£12,000	,, ,, ,, 3 per cent. Stock, 1972/74 ..	12,121	..	10,980
£3,000	Port of London 3½ per cent. Registered Stock, 1965/75 ..	2,687	..	2,805
£800	Ontario & Quebec Rly. 5 per cent. Permanent Debenture Stock	984	..	848
£4,000	Bankers Investment Trust Ltd., Deferred Stock	7,806	..	15,375
£3,250	Debenture & Capital Investment Trust Ltd., Ordinary Stock ..	6,586	..	11,213
£1,125	General Consolidated Investment Trust Ltd., Ordinary Stock ..	2,236	..	3,402
£3,750	London & Montrose Investment Trust Ltd., Ordinary Stock ..	7,893	..	11,500
£3,125	London Scottish American Trust Ltd., Deferred Stock ..	6,942	..	10,313
£625	London Scottish American Trust Ltd., Preferred Stock ..	—	..	578
£1,500	London Trust Co., Ltd., Deferred Stock	3,229	..	5,730
£1,180	Lowland Investment Co. Ltd., Ordinary Stock	2,683	..	3,475
£5,625	Mercantile Investment & General Trust Co. Ltd., Ordinary Stock	13,401	..	19,378
£5,000	Rio Claro Investment Trust Ltd., Ordinary Stock	11,192	..	16,625
£2,500	River Plate & General Trust Co., Ltd., Deferred Stock ..	7,691	..	9,875
£3,500	Sphere Investment Trust Ltd., Ordinary Shares	7,830	..	12,075
£1,739	Standard Trust Ltd., Ordinary Stock	3,025	..	5,739
£5,000	Sterling Trust Ltd., Ordinary Stock	8,731	..	15,625
£6,750	Third Guardian Trust Ltd., Ordinary Stock	8,663	..	13,331
£6,000	United States Debenture Corporation Ltd., Ordinary Stock ..	12,553	..	19,200
£6,000	Witan Investment Co. Ltd., Ordinary Stock	11,145	..	14,100
		£607,532		£665,713

SINKING FUND FOR FREEHOLD BUILDINGS.

£4,300	3 per cent. Funding Stock, 1959-69	3,876	..	4,365
£10,200	4 ,, ,, ,, 1960-90	9,079	..	10,506
£20,500	3½ per cent. Conversion Stock, 1961 or after	18,658	..	18,142
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	..	3,500
£10,000	,, ,, ,, 1960/70	9,623	..	9,600
£31,600	,, ,, ,, 1965/75	31,600	..	29,704
£2,000	2½ per cent. National War Bonds, 1954/56	2,107	..	2,005
£3,200	2½ per cent. Treasury Stock, 1975 or after	2,870	..	2,112
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	6,260	..	5,981
£3,000	,, ,, 3 ,, ,, ,, 1968/73 ..	2,916	..	2,850
£3,000	Third Guardian Trust Ltd., Ordinary Shares	3,000	..	5,925
		£93,507		£94,693

PENSION FUND.

Nominal Value		Balance Sheet Value		Market Value
£22,000	4 per cent. Funding Stock, 1960-90	£17,165	..	£22,660
£18,000	3½ per cent. Conversion Stock, 1961 or after	15,173	..	15,930
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	..	2,112
£1,000	3 ,, ,, ,, 1965/75	1,000	..	940
		£35,543		£41,642

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Stock, 1960/90	2,705	..	2,884
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986	..	1,738
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757	..	2,094
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097	..	994
		£8,545		£7,710

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3 per cent. Defence Bonds, Conversion Issue	1,000	..	1,000
£500	3 per cent. Savings Bonds, 1960/70	500	..	480
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	..	3,828
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903	..	841
		£7,606		£6,149

RE-ENDOWMENT FUND.

£5,400	3 per cent. Savings Bonds, 1960/70	£4,941	..	£5,184

The Lister Institute
of
Preventive Medicine

Report of the Governing Body
1955

Chelsea Bridge Road,
London, S.W. 1.

June 16th. 1955

THE GOVERNING BODY

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Deputy Director: Professor W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S.
Superintendent of Elstree Laboratories: W. d'A. Maycock, M.B.E., M.D.

MICROBIOLOGY, IMMUNOLOGY and EXPERIMENTAL PATHOLOGY

†A. A. Miles, C.B.E., M.A., M.D., F.R.C.P. (*Professor of Experimental Pathology in the University of London*).
Muriel Robertson, M.A., D.Sc., LL.D., F.R.S.
Emmy Klienebergér-Nobel, Ph.D., D.Sc.
D. L. Wilhelm, M.D.
P. J. Mill, B.A. (*Jenner Memorial Research Student*).
A. Felix, D.Sc., F.R.S. (*Public Health Laboratory Service*).
I. N. Asheshov, M.D. (*Medical Research Council External Scientific Staff*).
Elizabeth Hall Asheshov, M.Sc. (*Medical Research Council External Scientific Staff*).
J. F. Burke, M.D. (*U.S.A.*)
J. M. Elder, M.D., B.Sc. (*Canada*).

GUINNESS-LISTER RESEARCH UNIT

*B. A. D. Stocker, M.D., M.R.C.S., L.R.C.P.
C. J. Perret, M.A.
C. Quadling, B.Sc.

VIROLOGY.

L. H. Collier, M.D.

BIOCHEMISTRY

†W. T. J. Morgan, D.Sc., Ph.D., F.R.I.C., F.R.S. (*Professor of Biochemistry in the University of London*). *Principal Biochemist, Elstree.*
*Marjorie G. Macfarlane, D.Sc., Ph.D.
R. Côté, B.A., D.Sc.
Joan M. Mattingly, B.Sc., Dip.Bact.
G. Owen, M.B., Ch.B., B.Sc. (*Research Student*).
M. Ruszkiewicz, M.Sc. (*Research Student*).
Valerie Lawton, B Sc. (*Research Student*).
Winifred M. Watkins, B.Sc., Ph.D. (*Beit Memorial Research Fellow*).
J. V. McLoughlin, M.Sc. (*Medical Research Council Grantee*).
G. M. A. Gray, B.Sc. (*Medical Research Council Grantee*).
Dorothy J. Buchanan, Ph.D. (*U.S.A.*)

BIOPHYSICS

†R. A. Kekwick, D.Sc., (*Reader in Chemical Biophysics in the University of London*).
§Margaret E. Mackay, M.Sc., Ph.D. (*Medical Research Council External Scientific Staff*).
B. Cinader, B.Sc., Ph.D., (*Agricultural Research Council*).
P. Wolf, M.B., Ch.B. (*Medical Research Council Grantee*).
E. A. Caspary, B.Sc.
J. H. Pearce, B.Sc. (*Agricultural Research Council Grantee*).
Professor N. H. Martin, M.A., B.M., B.Ch., B.Sc. (*Honorary Research Associate*).

NUTRITION

§Dame Harriette Chick, D.B.E., D.Sc.
§E. Margaret Hume, M.A.

---

†Appointed Teacher of the University of London.
*Recognised Teacher of the University of London.
§Honorary Member of Institute Staff.

PREPARATION AND STUDY OF THERAPEUTIC SERA (ELSTREE)

B. G. F. Weitz, M.R.C.V.S.
J. Rodican, B.Sc.
Frances M. Lee-Jones, B.Sc.

PREPARATION AND STUDY OF SMALLPOX VACCINE (ELSTREE)

*D. McClean, M.B., B.S., M.R.C.S.
C. Kaplan, M.B., Ch.B., M.Sc.

PREPARATION AND STUDY OF BACTERIAL VACCINES (ELSTREE)

*A. F. B. Standfast, M.A., Dip.Bact.
Dorothy H. Card, B.Sc.
Doraine Thow, B.Sc.
Margaret E. Rowatt, B.Sc., Ph.D. (*Public Health Laboratory Service*).
Jean M. Horton, M.A., Ph.D. (*Medical Research Council External Scientific Staff*).

BLOOD PRODUCTS (ELSTREE)

*W. d'A. Maycock, M.B.E., M.D.
L. Vallet, M.A.
Shirley M. Evans, B.Sc.
Aileen J. Thompson, B.Sc.
Patricia A. Turner, B.A.

BIOCHEMISTRY (ELSTREE)

*D. E. Dolby, B.Sc., Ph.D.

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§R. R. Race, Ph.D., M.R.C.S., L.R.C.P., F.R.S.
Ruth Sanger, B.Sc., Ph.D.
Joan S. Sneath, B.Sc.

Blood Group Reference Laboratory.

§A. E. Mourant, M.A., D.Phil., D.M., M.R.C.P.
Dorothy M. Parkin, M.R.C.S., L.R.C.P.
Elizabeth W. Ikin, M.Sc.
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*Recognised Teacher of the University of London.
§Honorary Member of Institute Staff.

ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine

June 16th. 1955

REPORT OF THE GOVERNING BODY

The Governing Body has the honour to present its report of the work of the Institute for the year 1954/55.

GOVERNING BODY

The Governing Body has noted with pleasure the appointment, by Her Majesty the Queen, of the Earl of Iveagh to be a Knight of the Most Noble Order of the Garter.

In October last Professor S. P. Bedson, having represented the Royal Society for ten years, retired from the Governing Body. The Governing Body wish to record their appreciation of Professor Bedson's services as a Governor. The Governing Body welcomes Professor Wilson Smith as the new representative of the Royal Society.

At its last meeting the Council re-elected Sir Henry Dale, Sir Paul Fildes and Sir Wilson Jameson as its representatives on the Governing Body until 31st December, 1955.

COUNCIL

At last year's Annual General Meeting the three retiring members of the Council, Sir Alexander Fleming, Sir Henry Dale and Sir Howard Florey were re-elected.

The three members of the Council due to retire this year in accordance with the Articles of Association, but who are eligible for re-election, are Dr. G. S. Wilson, the representative of the University of London, Sir Merrik Burrell, the representative of the Royal Agricultural Society and Sir Wilson Jameson, a representative of the Members of the Institute.

The Governing Body learned with regret of the death on 16th February of Sir Charles Martin, Director of the Institute from November 1903 until December 1930. They record their deep sense of the great services which had been rendered to the Institute by Sir Charles Martin during his long and distinguished term of office as its Director, covering a critical period in the development of the Institute.

The Council have also lost two other distinguished members by the deaths of Sir Alexander Fleming and Sir Edward Mellanby.

MEMBERS

Professor N. H. Martin, Dr. B. A. D. Stocker and Mr. B. G. F. Weitz have accepted invitations to become Members.

The Governing Body records with regret the deaths of Dr. R. G. White and Dr. G. F. Petrie. Dr. Petrie joined the staff of the Institute in 1902 and in 1926 was appointed Bacteriologist-in-Charge at Elstree, a post which he retained until his retirement in 1939.

STAFF

At the end of 1954 Dr. J. Baddiley resigned on his appointment to the chair of Organic Chemistry at King's College, Newcastle-upon-Tyne. Miss J. Addey, Miss J. Bishop, Dr. R. A. Gibbons, Mrs. M. Gibbons, Mrs. L. Lam, Mr. K. B. Linton, Dr. A. P. Mathias, Dr. M. W. Schachter and Miss Sheehan also resigned during the year and Mr. G. Jamieson completed the tenure of his studentship.

Dr. Collier has taken charge of the new virus research laboratories established at Chelsea.

Dr. Coté, Miss V. Lawton, and Miss J. Mattingley were given temporary appointments in the Biochemical Department, Mr. J. A. Pearce in the Biophysics Department; Miss A. J. Thompson and Miss P. A. Turner in the Blood Products Laboratory at Elstree. Miss F. M. Lee-Jones also joined the Elstree staff to assist in the work undertaken on behalf of the Colonial Office. The Jenner Memorial Research Studentship was awarded to Mr. P. J. Mill.

The following visitors worked for short periods in the Institute laboratories: Dr. N. Ahad, Director, Pasteur Institute, Rangoon; Dr. D. Aminoff, Israeli Institute of Biological Research, Israel; Dr. F. Bozok, Turkish Red Crescent, Ankara; Dr. Clarice G. Crocker, Institute of Pathology, Pretoria; Dr. S. Dharmaraka, Research Section, Thai Red Cross; Dr. J. M. Dubert, Institut Pasteur, Paris; Dr. B. Melen, Sabbatsberg Hospital, Stockholm; Dr. F. Pötsch, Public Health Laboratory, Klagenfurt, Austria; Dr. R. F. Rao, Vaccine Institute, Belgaum, India; Dr. L. H. Rasch, Dusseldorf; Dr. J. Rüeher, Institute of Hygiene, Zagreb; and Dr. B. Sevgen, Turkish Red Crescent, Ankara.

Professor A. A. Miles attended a meeting of the expert committee on Biological Standardization of the World Health Organization at Geneva in October, 1954 and, at the invitation of the U.S. Army authorities, attended a symposium on Host Resistance at Frederick, Maryland, in November, 1954. As a member of the Executive Committee of the International Association of Microbiological Societies he attended the XIIth General Assembly of the International Union of Biological Societies in Rome, April, 1955. Professor W. T. J. Morgan opened a conference at Princetown, U.S.A., April, 1955, on "Polysaccharides in Biology," sponsored by the Josiah Macy Foundation. At the invitation of the Société Internationale de Transfusion Sanguine, Professor W. T. J. Morgan, Dr. R. A. Kekwick and Dr. W. d'A. Maycock took part as chairmen of sessions in the Fifth International Congress on Blood Transfusion, Paris, September, 1954. At the invitation of the Centre Internationale de l'Enfance, Dr. R. A. Kekwick took part in a symposium on gamma globulin held in Paris, 1954. At the invitation of the International Union against the Venereal Diseases and Treponematoses Dr. Klieneberger-Nobel took part in a Symposium on Non-gonococcal Urethritis, Monaco, June, 1954.

Dr. J. Baddiley was awarded a Rockefeller Special Fellowship for three months study in the U.S.A. and at the invitation of the American Association for the Advancement of Science took part in the Gordon Conference on Vitamins and Metabolism, August, 1954.

Dr. W. d'A. Maycock has been appointed as a War Office representative on the N.A.T.O. Committee of Experts dealing with the standardisation of transfusion equipment.

The Governing Body notes with satisfaction the successful continuance of the researches under Professor Miles and Professor Morgan, which is made possible by the generous benefaction of the Nuffield Foundation.

The Blood Group Research Unit and the Blood Group Reference Laboratory of the Medical Research Council are still accommodated at the Institute.

MICROBIOLOGY.

Hæmophilus pertussis Antigens. Mr. Standfast and Dr. Jean Horton have continued their work on the protective antigens of *Hæmophilus pertussis* for mice.

A survey of a number of the rabbit antisera to *H. pertussis* cells and various fractions thereof revealed the existence of two distinct antibodies, one passively protecting mice against lethal infection by the intra-cerebral route, the other passively protecting mice against lethal infection by the intranasal route. Neither is the antitoxin. Antisera against S forms of *H. pertussis* contain both types of protective antibody.

The fractions of *H. pertussis* obtained by ethanol precipitation of (*a*) phenol extracts and (*b*) tryptic digests of the cells each contain at least two antigens; in each case one of the antigens is common to both fractions. The tryptic digest fraction actively immunizes mice against lethal intracerebral infections, but not against lethal intranasal infections. The phenol extract fraction immunizes against both, though more effectively against the intracerebral infection. Antisera to both fractions protect mice passively against intracerebral but not intranasal infections.

The course of sublethal infection of mice by the intranasal route is being studied by estimating the content of viable bacilli in the lung.

Dr. Margaret Rowatt continued investigations of the growth of *H. pertussis* in liquid media. Growth from small inocula was always obtained by sterilizing the cysteine of the medium by filtration instead of autoclaving.

Growth rate and metabolism of amino acid in growth were measured on strains of *H. pertussis*, *H. parapertussis* and *H. bronchisepticus*. Glutamate was the first amino acid to be used, and an equivalent quantity of ammonia was formed by each species. Washed suspensions of the three species oxidised glutamate, but, in this case, less ammonia was formed than glutamate was used. In *H. parapertussis* some of the nitrogen appeared as arginine and

ornithine. These compounds were not formed by the other two species and no other nitrogen-containing compound was found. *H. bronchisepticus* contained glutamic decarboxylase but the other two species did not.

Mr. Standfast, Miss Kathleen Cook and Miss Doraine Thow, in conjunction with Dr. J. O. Irwin of the M.R.C. Statistical Unit, have finished their investigation of the intracerebral mouse test for potency of whooping cough vaccine and this work is now being prepared for publication; it was carried out for the Medical Research Council Whooping Cough Committee.

Typhoid Bacillus Antigens. Mr. Standfast, Miss Horton and Miss Thow have started an investigation of mouse tests for assaying the potency of typhoid vaccines as part of a collobora-tive study initiated by the World Health Organisation.

Vole bacillus. Miss Dorothy Card has continued her investigation of the growth requirements of *Mycobacterium tuberculosis* var *muris*.

Bacterial Genetics. Dr. Stocker, assisted by Mr. Quadling, has continued his researches on genetic transduction in *Salmonella*. Pedigree studies on individual cells made motile by transduction, and isolated by use of the micromanipulator, have clarified the phenomenon of "abortive transduction"; that is, the transfer of a new character to a bacterial cell which, however, fails to transmit this character to all its progeny. It seems that, as has been suspected earlier, a phage-imported fragment of genetic material conferring the ability to make flagella (and so to be motile) may fail to replace in the recipient cell the "allele" determining failure to produce flagella, and that such a supernumerary fragment is never replicated, but is transmitted unaltered to a single one of the descendants of the original cell. In pedigree experiments the unique gene-bearing descendant has been identified and isolated from amongst the progeny of the 14th generation. A phenomenon which had not been suspected, and which for long made difficult the interpretation of the pedigrees, is that a cell unable to manufacture flagella is none the less able to operate, and to transmit to its progeny, any "motility-conferring particles" it may have received from its parent. Such non-multiplying particles, presumably flagella or granules which secrete them, have been traced in pedigrees through as many as 20 generations.

Mr. Quadling has begun a study of the small proportion (probably less than 1 in 10^5) of motile cells which occur spontaneously in some non-motile strains of *Salmonella* species; such cells have been isolated by micro-manipulator, and shown not to be stable mutants, because all, or nearly all, their progeny are non-motile; but the detection of from one to five motile cells amongst the decendants many generations later indicates that motility-conferring particles synthesised by the original variant cell are transmitted to its descendants, which, however, are unable to manufacture further particles.

Other work on the genetics of flagellar characters in *Salmonella* species includes a disproof of a hypothesis used earlier in the attempted mapping, in linear order, of certain genes; there is therefore now no positive evidence for a linear gene order in *Salmonella* species.

In collaboration with Dr. G. G. Meynell, at the British Post-graduate Medical School, experiments on infection of mice with mixtures of genetically "tagged" variants of *S. paratyphi B* and *S. typhi-murium* have been continued.

Bacterial Chemistry. Mr. Perret has investigated the kinetics of growing bacterial populations. For the study of penicillinase adaptation in *Bacillus cereus*, two chemically defined media for the continuous culture of *B. cereus* were devised; a glucose inorganic salts basic mixture augmented in one case with aspartic acid, arginine and cystine, and in the other with glutamic acid, histidine, methionine and glycine.

It appeared that refined versions of the iodometric penicillinase assay might be suitable for measurements of the adaptation of single bacteria, and so permit comparison between individuals drawn from a 'homogenous' population. A variation based on the partition of ^{131}I between CCl_4 and water was developed to the limit imposed by non-specific iodine reduction; it was then about 10,000 times more sensitive than standard assays and could detect about 4×10^{-19} Mol. of penicillinase. Though a fully adapted bacterium of *B. cereus* (strain NRRL 569) can produce about 5×10^{-20} Mol., a non-adapted cell produces only about 10^{-23} Mol. of enzyme. The further necessary 100 fold increase of sensitivity of the assay unfortunately proved impossible to attain.

For the study of the relationship between generation time and the life cycle of *Escherichia coli*, a new pattern of continuous culture apparatus has been constructed. Designed for operation in a Warburg tank, it is capable of maintaining 8 cultures at constant density and different growth rates at the same time. Assembly, replenishment and the selection of either of two different media can be readily accomplished under sterile conditions. *E. coli*, strain K 12, has been grown in the apparatus on a glucose limited synthetic medium at generation times fixed between 1 and 8 hours. Preliminary differential counts of samples under the phase contrast microscope support the hypothesis that increasing the generation time disproportionately extends the inter-division period of the bacterial life cycle.

Organisms of the Pleuropneumonia Group. Dr. Emmy Klieneberger-Nobel has continued the morphological investigations of organisms of the pleuropneumonia group and L forms of bacteria by electronic microscopy in collaboration with Mr. F. W. Cuckow and Mr. M. S. C. Birbeck of the Chester Beatty Institute. Electron micrographs of various organisms in liquid and on solid media have been obtained by specially devised methods. Examinations of colonies by ultra-thin sections are in progress; and it is planned to use the technique for the study of tissues infected with pathogenic members of this group of organisms. Filtration studies of pleuropneumonia-like organisms and L forms of bacteria have been continued.

With Dr. K-K. Cheng, at the Medical Research Council Toxicology Research Unit, Serum Research Institute, Carshalton, Dr. Klieneberger-Nobel studied the relationship between the development of bronchiectasis after bronchial ligature and the appearance of the pleuropneumonia-like organism "L3" in rats.

Investigations are in progress of the significance of pleuro-pneumonia-like organisms in "non-specific" genital infections and of the optimal conditions of their cultivation from pathological material.

Bacteriophage Typing. Dr. Felix has continued his work on typing of typhoid and paratyphoid bacilli by the bacteriophage method. He has co-ordinated the collaborative investigations of various theoretical and practical aspects of this problem, that are being conducted in different countries by members of the International Committee for Enteric Phage Typing of which he is joint chairman and secretary.

Bacterial Viruses. Dr. Dolby has continued the study of substances inhibiting the multiplication of the T series of bacteriophages in *Escherichia coli B*. Cyanide and arsenite permanently inhibit virus multiplication, whereas borate inhibits temporarily, with a consequent increase in the length of the latent period without alteration of the final yield of virus. These results have been explained by the hypothesis that cyanide and arsenite block the anærobic pathway of carbohydrate metabolism in *E. coli*, which is essential for virus multiplication; whereas borate blocks the ærobic pathway which is not essential and which in fact is suppressed when the bacteria are infected by bacteriophages of the T series.

Dr. Stocker has detected a new kind of phage-resistant mutant of *E. coli B*; by the use of this mutant it is possible to detect a new class of host-range mutants in phage T1. Several such phage mutants are being investigated, in the hope of discovering what kind of alteration of the bacteriophage particle enables it to attack a resistant host.

Antibiotics active against Bacterial Viruses. After a survey of substances from several actinomycetes showing antiphage activity, Dr. Asheshov concentrated on the study of one of them, A220, which produces a group of closely related substances (rutilantins) active against several bacteriophages. By a new method of concentration and purification the active material was purified forty-fold. Different fractions are being studied chromatographically, and their biological properties are being studied by Mrs. Elizabeth Asheshov.

Another antibiotic, aklavin, was submitted to other laboratories for tests against animal viruses. Dr. E. Weston Hurst of the Virus Department, Imperial Chemical Industries, Blackley, observed an apparent inactivation of the virus of Eastern Equine Encephalomyelitis *in vitro*. Dr. L. Hoyle of the Public Health Laboratory Service, General Hospital, Northampton, found that it had no virucidal effect on influenza virus, but retarded and reduced virus multiplication in egg, in all probability by interfering with nucleoprotein synthesis.

Mrs. Asheshov has concluded a study of the inducing action of phagolessin A58 on lysogenic strains of bacteria.

Vaccinia Virus. Dr. Collier, Dr. McClean and Mr. Vallet have completed their study of the antigenicity in rabbits and monkeys of vaccinia inactivated by ultra-violet light. There is a logarithmic relation between exposure to irradiation and destruction of virus, which can be used to indicate the exposure necessary to produce complete inactivation. Excessive exposure rapidly destroys the antigenicity of the preparations.

Confirmatory experiments in which the tests for inactivation of the virus were more than usually stringent provided the expected protection of rabbits; no living virus was detected in the equivalent of 80 millilitres of the suspension which was used in two immunizing doses of 2 millilitres. It is intended to find out whether the results obtained in animals can be reproduced in human volunteers, in the hope of providing a basal immunity in those subjects not suitable for vaccination with living virus.

The first stage of an international investigation into the potency, purity and stability of dried smallpox vaccines from various sources, under the auspices of the World Health Organization, was completed in 1954. This investigation, in which the Smallpox Vaccine Unit of the Institute collaborated with laboratories in Copenhagen and Paris, was confined to laboratory assays of the vaccines after storage for various periods at different temperatures up to 45°C. The second stage of this investigation is now in progress; this comprises combined laboratory and clinical trials under field conditions on two dried vaccines after similar periods of storage at different temperatures. Professor A. W. Downie of the Bacteriology Department, Liverpool University, is collaborating with the Institute in the titration of these samples of vaccine. Apart from information on the stability of dried smallpox vaccine, this investigation should yield much needed information about the immunity following its use and the correlation between potency titrations by various methods in the laboratory and percentage "takes" in vaccination.

The Lister Institute Dried Smallpox Vaccine is now in active use in the field.

Dr. Kaplan is studying the neurotoxicity in the mouse of preparations of non-neurotropic vaccinia virus. In this connection he is investigating the suitability of intra-cerebral inoculation in mice of virus-serum mixtures for the titration of the neutralizing activity of anti-vaccinial sera.

In collaboration with Dr. R. E. Billingham of the Zoology Department, University College, London, Dr. Kaplan has begun an investigation of the antibody responses in maturity of animals injected with antigens in embryonic life It is intended that this research should include the study of virus antigens in animals susceptible, and also naturally resistant, to infection with the relevant viruses.

The precision of titration of vaccinia virus by pock counting on the chorio-allantois of the chick embryo is being re-investigated by Dr. Kaplan in collaboration with Dr. Collier and members of the Medical Research Council Statistical Unit.

Protozoology. Dr. Muriel Robertson is completing her study of *Trichomonas foetus* in collaboration with Dr. W. R. Kerr (Department of Veterinary Research, Ministry of Agriculture, Northern Ireland). The impairment of immunological response to *T. foetus* freeze dried antigen induced in calves by injection of large doses of this antigen during the first three weeks of life, has persisted in animals up to the age of twenty-five months.

The analysis of the two serological varieties of *T. foetus* by the gel-diffusion method of Ouchterlony has progressed. Certain of the antigens revealed by the method are common to both, but those in the polysaccharide fractions are quite distinct.

The study of antigenic fractions of strains of the *Tetrahymena* species by the same method is continuing.

PATHOLOGY.

Plasma Substitutes. Dr. Maycock, with Mrs. Lam and later Miss Patricia Turner, continued the investigation of the distribution of intravenously injected dextran in the tissues of the mouse.

Dr. Maycock and Miss Turner undertook, on behalf of the Medical Research Council Dextran Working Party, an investigation of the renal excretion and persistence in the blood stream of certain types of dextran.

Pharmacology of Serum Fractions. Professor Miles, Dr. Schachter, Dr. Mackay and Dr. Wilhelm have completed the broad characterization of certain large-molecular substances present in guinea-pig serum, that have pharmacological effects on the blood vessels of guinea-

pigs and other mammals. Fresh guinea-pig plasma and serum contains the inactive precursor of an α_2-globulin, which on dilution of serum with saline or during ether-fractionation is transformed into a very active, relatively heat-stable factor, PF, that increases the permeability of the blood capillaries. One millilitre of serum yields about 1 milligram of PF, which is as active as histamine on a weight basis and 2,000 times as active on a molar basis; this PF also causes hypotension in the guinea-pig, cat and dog and leucocytosis in guinea-pig skin. The PF is distinct from fibrinolysin and is not a histamine-liberator. Its ready inhibition by soya bean trypsin inhibitor suggests that PF is a protease.

Guinea-pig serum also contains a slowly-acting, heat labile substance, that inhibits PF; it is an α_1-globulin.

A second permeability-increasing factor matures in ageing serum, but less than 0·5% of the permeability-increasing potency activable in serum can be attributed to this factor.

Dr. Wilhelm, Professor Miles, Dr. Elder and Mr. Mill have extended this investigation to substances with PF activity in human, rat and rabbit sera, tested in the homologous species and in guinea-pigs. The PF preparations obtained from the sera of these species are less potent than that from guinea-pig serum, but are similarly susceptible to guinea-pig serum inhibitor preparations and to soya-bean trypsin inhibitor.

Mr. Mill is exploring methods of demonstrating *in vitro* the enzymic activity of permeability factors and their inhibitors present in these mammalian sera. Dr. Elder is also investigating permeability factors by means of the wheal and flare reaction in human skin.

Capillary Permeability. Dr. Wilhelm and Professor Miles have studied histological changes in capillary endothelium induced by various permeability-increasing substances; and continued the investigation of morphological changes in inter-endothelial cement of large veins after treatment with similar substances.

In collaboration with Dr. Marjorie Macfarlane, Dr. Elder and Professor Miles are investigating the time-relations of pathological increase in capillary permeability induced in the guinea-pig by toxic filtrates from cultures of the gas-gangrene clostridia; and so far have tentatively identified the α-toxins of both *Cl. welchii* and *Cl. oedematiens* as the active subtance in these two organisms.

The Primary Lodgement of Infective Bacteria. Dr. Burke and Professor Miles are investigating the vascular reactions in terms of both blood and lymphatic vessels of the guinea-pig skin to a number of common pathogenic bacteria, during the first few hours of infection. By the use of various pharmacological substances, including enzyme-inhibitors, they are attempting to estimate the defensive value of the humoral and cellular reactions to these local infections.

SEROLOGY AND IMMUNOLOGY.

Standardization of Diagnostic Agglutination Tests. Dr. Felix has co-operated with Lt. Col. H. J. Bensted of the Standards Laboratory for Serological Reagents, Colindale, and with Dr. O. Maaløe of the Statens Serum Institut, Copenhagen, in the organization of the collaborative assays of seven Standard Agglutinating Sera for typhoid and paratyphoid A and B bacteria that have been prepared for the Section of Biological Standardization of the World Health Organization.

Identification of Insect Blood Meals. Mr. Weitz and Miss Janet Bishop have continued their research on the identification of serum proteins of closely allied species of mammals by means of the inhibition of agglutination test, using suspensions of tanned red blood cells sensitized with serum proteins of different animals as indicator particles. Confirmatory experiments gave sufficiently accurate results to warrant the testing of tsetse fly blood meals from a wide variety of sources in East Africa. When these surveys are completed, the results should yield, for the first time, accurate information on the feeding habits of various species of *Glossina*.

Using a similar technique, a quantitative method for the determination of serum protein fractions has been devised. By this means, it is intended to study the species-specificity of serum protein fractions and the rates of digestion of such fractions in various species of blood-sucking insects.

Antitoxins. Dr. Dolby has continued his studies on the removal of inactive proteins from antitoxic sera by low-temperature alcohol fractionation and by the use of a combination of cresol and ammonium sulphate precipitation. Work on the application of these methods to large scale purification of antitoxic sera has begun.

He has devised a method for the purification of crude pepsin by adsorption on calcium phosphate and elution with citrate buffers, which gives a product with a purity approaching that of crystalline pepsin and a yield of 60-70% in large scale experiments. Further work on the fractionation of this product is in progress.

Toxin-Antitoxin Reactions. Mr. Rodican is investigating the methods of preparation of various clostridial toxins, and the assay of tetanus antitoxin by flocculation methods.

Serology of Enzymes. Bovine ribonuclease has been fractionated by chromatography by Dr. Cinader and Dr. Rondle. With Mr. Pearce, Dr. Cinader has demonstrated the existence of a non-enzymic antigen in crystalline ribonuclease preparations. Ribonuclease A and B, described by Moore and Stein as constituents of crystalline ribonuclease, could not be distinguished immunologically. The inhibition of the enzyme by rabbit antibody has been examined by a manometric method.

Inhibition of Immune Response. Dr. Cinader and Dr. Dubert have investigated the inhibition of the immune response in rabbits by the injection of human serum albumin at birth. Animals from three litters were injected with serum albumin at birth, and later when adult, the latter injections being followed subsequently by injections of diazo-sulphonic human serum albumin and tobacco mosaic virus. In all but one of the control animals antibody to human serum albumin could be demonstrated by flocculation tests, diffusion in agar gels and the agglutination of tanned erythrocytes. No antibody to human serum albumin could be detected in any of the animals injected at birth, and in these animals the antigen could be demonstrated in the circulation of the adult animal four days after the injection of human serum albumin. Of the animals with acquired tolerance to human serum albumin so far tested, all have produced antibody to tobacco mosaic virus, but only one has produced antibody to diazo-sulphonic human serum albumin.

The cross reactions between diazo human serum albumin, diazo bovine serum albumin and diazo rabbit serum albumin and the corresponding native serum albumins have been examined by agar diffusion against antibodies to human serum albumin and diazo human serum albumin.

BIOCHEMISTRY.

The Human Blood-group Substances. Professor Morgan and Dr. Winifred Watkins have studied the inhibiting action of simple sugars on the enzymes which decompose blood group substances with a view to characterizing the enzymes destroying the serological activity of the A, B and H substances. Destruction of A-substance by enzyme preparations from *Trichomonas foetus* or *Cl. welchii* was inhibited almost completely by *N*-acetylgalactosamine and its methyl glucoside, and to a very slight extent by D-galactose, but not by any of the other sugars included in the test. If it is assumed that the enzyme is inhibited by a product of its own reaction it appears that the initial change leading to loss of A serological activity involves the hydrolysis of an *N*-acetylgalactosamine linkage. Destruction of B substance by the *T. foetus* enzyme, on the other hand, was inhibited only slightly by *N*-acetylgalactosamine but the same concentration of D-galactose and galactopyranosides inhibited the action of the enzyme almost completely. The enzyme destroying B serological activity therefore appears to be a galactosidase. Partially purified H-destroying enzymes from *T. foetus* and *Cl. welchii* were inhibited by L-fucose and D-galactosamine. The importance of L-fucose in determining H-specificity had been suggested earlier by the results of serological inhibition tests using the H agglutinins in normal eel serum and certain plant seeds.

Dr. Watkins has continued to study methods for the purification of the enzymes obtained from *T. foetus* which destroy the serological activity of the human blood group substances and has examined the chemical changes associated with enzymic degradation of the H substance. Reducing sugars are liberated and part of the material becomes diffusible through a cellophan membrane. The *T. foetus* enzyme primarily liberates L-fucose from the H-substance together with a small amount of *N*-acetylhexosamine. No liberation of galactose was detected.

The methyl glycosides of L-fucose were prepared as possible synthetic substrates for the *T. foetus* enzyme. The furanosides, which have not previously been described, were prepared by boiling L-fucose with a very dilute solution of methanolic HCl, and separated on a column of powdered cellulose. α-Methyl L-fucofuranoside was isolated in crystalline form and β-methyl L-fucofuranoside as a syrup which has so far failed to crystallise.

Dr. Owen has continued his work on the isolation of the blood group specific substances present in meconium. It was not possible to isolate a homogeneous material by the techniques used for cyst blood group substances. Electrophoresis revealed a second component in all preparations. Some of the newer techniques such as adsorption chromatography, ion exchange and zone electrophoresis have been applied with a view to obtaining the two components in an electrophoretically homogenous condition.

Attempts to produce anti-'Lewis' (group Le^a) sera in rabbits, using purified Lewis (Le^a) substance coupled with a conjugated (lipo) protein of bacterial origin, were unsuccessful.

Mr. Ruszkiewicz is attempting the isolation from cyst fluids of human origin of homogeneous mucoid materials with serological reactivity. The materials are required for oxidation studies with periodate since it is believed that the examination of the products of the oxidation of the blood group substances will indicate the presence of certain chemical structures in these important biological materials. Mr. Ruszkiewicz has devised a method for removing interfering ions from carbohydrates after oxidation by treatment with an anion exchange resin and has extended the use of this technique to the estimation of formaldehyde produced after oxidation of simple sugars and blood group substances.

Dr. Dorothy Buchanan has extended some earlier observations, made by Dr. Crumpton, on the enzymic decomposition of blood group substances of animal and human origin. Using an enzyme preparation obtained from *Cl. welchii* it has been found that fucose, galactose and *N*-acetylhexosamine, in the proportion of 13 : 10 : 12, and a small amount of an amino sugar-containing disaccharide are liberated. *N*-acetyl-glucosamine is split off preferentially. The reactivity of the H-specific mucoid when measured with most rabbit and human anti-H sera is destroyed, but titration with an anti-H serum "Warboys" of human origin indicates that no destruction of H-character has taken place. It seems that a 'core' of the native H-mucoid possesses full serological activity against this particular anti-H serum and that the 'Warboys' serological character of the H-substance does not depend on the presence of those sugars liberated by the enzyme, which include the "acid-labile" fucose.

Dr. Buchanan has made an immunological analysis of the reaction of the "O" somatic antigen, and the specific haptens of *Shigella dysenteriæ* by means of the Ouchterlony and Oudin techniques.

Bacterial Antigens. With Dr. D. A. L. Davies, of the Microbiological Research Department, Porton, Professor Morgan has completed a study of the specific polysaccharide haptens of the dominant 'O' somatic antigen of *Shigella dysenteriæ*. The degraded polysaccharide hapten $(\alpha)_D^{20}+98°$; N, 1·9%, obtained from the isolated antigenic protein-polysaccharide complex contains acetyl-glucosamine (27·5%), rhamnose (33%) and galactose (27%). No P was present. The molecular weight of 25,000-28,000 by end group assay and 26,000 by sedimentation and diffusion measurements, shows the identity of the chemical and physical units. The degraded polysaccharide is neither toxic nor antigenic, but is pyrogenic in relatively large doses, (2-5μg./kg.). The undegraded polysaccharide, $(\alpha)_D^{20}+94°$; N, 2·2%, extracted from the organisms with diethylene glycol differed from the degraded material in containing a few per cent of amino acids, and in having a molecular weight of the order of one million by sedimentation and diffusion measurements. The material is poorly toxic (mouse LD_{50}, 400μg.), is weakly antigenic and is less active as pyrogen, (0·05 μg./kg.), than the lipopolysaccaride or complete antigen. The lipopolysaccharide, $(\alpha)_D^{20}+95°$; N, 2·04%; P, 0·8% extracted from the isolated antigenic protein-polysaccharide complex with phenol contains about 7% of chloroform-soluble, ether-insoluble phospholipid. The lipopolysaccharide is of a very large particle size, is toxic, (mouse LD_{50}, 80μg.), and is a strong heterophile (Forssman) antigen, but weakly active in inducing the formation of specific agglutinins and precipitins in the rabbit. The material is also a very powerful pyrogen, active at 0·002 μg/kg. in the rabbit.

Toxins and Enzymes. Dr. Marjorie Macfarlane has continued her work on various aspects of the biochemistry of bacterial toxins. Work previously reported suggested that differences in the velocity of action of a potentially toxic enzyme towards different kinds of cells could be ascribed to the goodness of fit between particles of specific structure and might be a basic factor in determining virulence. In collaboration with Dr. Dolby, lecithinases derived from strains of *Clostridium welchii* which vary extremely in virulence towards guinea-pigs are now being examined. In relation to their enzymic activity towards aqueous lecithin, the lecithinase (alpha-toxin) derived from a highly virulent strain, 5053, is more lethal in mice and has a greater hæmolytic capacity towards guinea-pigs red cells than the lecithinase of an avirulent strain 3895. Both lecithinases are neutralised by the standard *Cl. welchii* antitoxin ; but there is apparently a difference in structure between the strain-specific toxins which determines a difference in their affinity for specific red cells. This affinity can be expressed as the apparent Michaelis constant of the hæmolytic system by determining the velocity of hæmolytic action at different concentrations of red cells. This finding has interesting implications with regard to the difference in virulence of different strains of other toxigenic organisms. This investigation is being extended to other strains of *Cl. welchii*.

Dr. Macfarlane, continuing experiments on the effects of *Cl. oedematiens* toxin on tissue constituents, found that samples of *Cl. oedematiens* Type B toxins contained an antigenic sulphydryl-activated enzyme, which decomposes the muscle proteins tropomyosin and actomyosin. Neutralisation tests with selective antisera showed that the antigen is distinct from those previously detected in *Cl. oedematiens* toxins, and it has therefore been designated as *Cl. oedematiens* eta-antigen. This enzyme has been detected also in a *Cl. hæmolyticum* toxin, but not in *Cl. oedematiens* Type A toxins.

Miss Macfarlane, with the assistance of Mr. Gray, is examining methods for the isolation of the so-called acetalphospholipids, which form a substantial proportion of the phospholipids of many tissues but whose constitution and function is largely unknown. It is intended later to study particularly the susceptibility of these compounds to toxic factors.

Coenzyme A. Continued efforts were made by Drs. Baddiley, Buchanan and Thain towards a synthesis of dephospho-coenzyme A. Several partly protected derivatives of pantetheine-4′-phosphate have been prepared and attempts have been made to condense these in pyrophosphate linkage with derivatives of adenosine-5′-phosphate. Highly complex mixtures were obtained after removal of protecting groups but it is likely that one of the minor components is the desired dephospho-coenzyme A. Further investigation of this synthesis is in progress.

Cytidine Nucleotides from Lactobacillus arabinosus. Dr. Baddiley and Dr. Mathias isolated milligram quantities of the two cytidine nucleotides they discovered in *L. arabinosus*. The two compounds have very similar properties and the analysis of the purified sample proved that they are both derivatives of cytidine-5′-pyrophosphate. The nature of the other parts of these compounds is not yet clear. On hydrolysis in acids both yield cytidine-5′-phosphate and an organic phosphate which is different in the two cases.

Active Methionine. Full confirmation of the structure of the product of enzymic demethylation of active methionine was obtained by Dr. Baddiley and Mr. Jamieson. Adenosylhomocysteine was synthesised by an unambiguous route and was shown to be identical with the natural product formed from active methionine during transmethylation. Direct methylation of adenosyl-homocysteine with methyl iodide gave active methionine itself in reasonable yields.

Nucleotide Precursors. The stages involved in the biosynthesis of purine nucleotides is becoming clear from investigations on the fate of simple known precursors in pigeon liver extracts. In this way it has been shown by American workers that ribose-phosphate derivatives of glycineamide and imidazoles are formed as intermediates in purine nucleotide synthesis. Drs. Baddiley, Buchanan, Handschumacher and Hodges hope to confirm the structures tentatively assigned to these ribose derivatives by chemical synthesis and also to elucidate the nature of some of the as yet unknown intermediates.

A synthesis of the two model substances, 1-glycylaminoglucose and 1-formylglycylaminoglucose, was achieved. These behave chemically in a very similar manner to the two nucleotide purcursors, 1-glycyl-aminoribofuranose-5-phosphate and its formyl derivative, thereby supporting the current views on the early stages of nucleotide bio-synthesis.

Sugar Phosphates. Drs. Baddiley, Buchanan and Szabo continued their studies on cyclic sugar phosphates. It was found that glucose-4:6 cyclic phosphate very readily undergoes an Amadori rearrangement with *cyclo*hexylamine to give 1-*cyclo*hexylamino fructose cyclicphosphate in which, for steric reasons, an open chain structure is present. The constitution of certain known cyclic phosphates was revised in the light of these findings.

BIOPHYSICS.

Human Plasma Proteins. Studies of the various protein fractions separated from normal human plasma by the ether method of Kekwick and Mackay, have been extended with a view to isolating individual constituents from some of the main fractions in more purified form, by the development of subfractionation procedures.

Human fibrinogen, already isolated in a high state of purity, is being intensively studied from a physico-chemical point of view by Mr. Caspary. Preparations examined by the isoelectric spreading of the boundary in the electrophoresis apparatus reveal a slight degree of electrochemical heterogeneity; ultracentrifuge studies of the size distribution in such preparations are also in progress.

When more than 30% of the free amino groups of fibrinogen are acetylated with 2'-acetyl thio-ethylacetamide, the formation of a clot with thrombin is prevented. It has been established that peptides are liberated from such acetylated fibrinogen by thrombin, as with native fibrinogen. That the acetylated fibrinogen does not form a clot must therefore be due to the inhibition of the polymerisation which normally follows the peptide splitting reaction with thrombin.

The supernatant solution obtained after precipitating the fibrinogen fraction from normal human plasma with ether is very similar in its clotting characteristics to defibrinated hæmophilic plasma. Dr. Wolf has developed an assay method for antihæmophilic globulin, utilising this supernatant solution as a test substrate, and this method is being used to improve the recovery of antihæmophilic globulin from normal human plasma and to devise methods for its purification. Results obtained suggest that the passage of plasma through a paper pulp filter, which has been an early step in the bulk fractionation procedure, causes a loss of some 25% of the antihæmophilic activity, probably by inactivation or consumption rather than by adsorption. It is also clear that antihæmophilic globulin rapidly loses activity when solutions containing ether are maintained at room temperature.

The prothrombin fraction separated next from human plasma, following the removal of the fibrinogen fraction, contains, in addition to prothrombin and prothrombin conversion accelerator factors, most of the plasma plasminogen. By adsorption on to barium sulphate the prothrombin has been removed from the fraction. It can be eluted subsequently and readily converted to thrombin, providing a preparation substantially uncontaminated with plasminogen. The further purification of both thrombin and plasminogen made possible by this initial step is being pursued by Dr. Mackay and Dr. Kekwick.

By measurements of sedimentation coefficient and diffusion coefficient with highly purified gamma globulin, Mr. Caspary has redetermined the molecular weight obtaining a value of 166,000 $\pm$ 6,000. The material used showed some electrochemical heterogeneity.

In preparations of gamma globulin from U.S.A. the presence of substantial amounts of ill-defined components with sedimentation coefficients between 8-12 *S* in addition to the main component (7 *S*) has frequently been reported. These 8-12 *S* components are not apparent in whole plasma. Recently, in preparing large pools of gamma globulin for poliomyelitis prophylaxis, aged plasma was used, and this gamma globulin contained components with sedimentation coefficients in the range 8-12 *S*. It appears that these components develop with ageing of liquid plasma; such components do not occur in gamma globulin prepared by the ether method from fresh (24 hr.) normal human plasma.

Professor N. H. Martin has continued studies of anomalous serum proteins occurring in disease processes, with special reference to the characteristics of the gamma globulins from sera of patients with hyperglobulinemia of apparently diverse ætiology.

BLOOD.

Blood Products Laboratory. During the past year the staff was fully engaged in bringing the new laboratory at Elstree into use. All sections of the laboratory, save one, which will remain temporarily at Chelsea, had begun work in the new laboratory at the end of 1954.

During the period of transition the preparation, for the Ministry of Health, of dried human plasma was maintained, but the production of plasma fractions and derivatives had to be diminished and, in the case of one fraction, temporarily stopped.

It is expected that the laboratory will come into full use during the next two years.

Mr. Vallet has supervised the installation of most of the new laboratory equipment and its preliminary trial before routine use. He has made further observations on the technique of irradiation of vaccinia with ultra-violet light.

Miss Shirley Evans has investigated the use of paper electrophoresis for the control of plasma fractionation.

Blood Group Research Unit. Once again much of the year's work has been done in collaboration with friends in the United States. The genetic phenomenon known as "position effect" has been illustrated in Man by the Rh blood groups. With the help of Dr. T. J. Greenwalt, of Milwaukee, and of Dr. A. Cahan, of New York, we have been able to investigate negro blood groups. Negro blood is disclosing itself as being unexpectedly different from that of whites. The differences now being studied are not those of frequency distribution, which have long been recognized, but differences of kind: new allelomorphs have been found in the MNSs, Rh and Duffy systems. It seems that negro blood may provide us with much interesting work for the future.

Mrs. Joan Sneath, in collaboration with Dr. P. Sneath of the National Institute for Medical Research, has demonstrated that the somewhat mysterious Lewis blood group antigens can be "caught" from plasma—a phenomenon already observed with one of the many blood group systems in cattle.

The Unit is collaborating with Dr. Sheila Callender of the Nuffield Department of Clinical Medicine, Oxford, in a genetical and hæmatological study of pernicious anæmia; and with Dr. Eliot Slater and Mr. J. Shields of the Maudsley Hospital, in twin investigations, and with Dr. J. N. Marshall Chalmers, of St. George's Hospital, in work on sickling of red cells.

The Unit is greatly indebted to the Blood Group Reference Laboratory for a most generous supply of antisera and to Professor Sir Ronald Fisher, F.R.S., for continued help and encouragement.

Blood Group Reference Laboratory. The ever-increasing supply of numerous varieties of blood grouping serum to laboratories in Great Britain and abroad has continued. Further help has been given to laboratories setting up their own testing services, by the supply of diagnostic sera and by the detailed testing of the red cells of their staff members. The routine work of testing red cells and pathological sera has continued, and various rare hæmagglutinating sera have been identified by applying a variety of techniques, including the use of proteolytic enzymes.

Studies have been carried out of the blood groups of four Sudanese tribes, and of the Veddahs of Ceylon.

Dr. Dorothy Parkin has continued her work on rare and familial blood group antigens.

Miss Elizabeth Ikin has continued to investigate the behaviour of rabbit sera which agglutinate red cells containing fœtal hæmoglobin.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

PAUL FILDES,

Acting Chairman of the Governing Body.

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THE LISTER INSTITUTE OF PREVENTIVE MEDICINE

Balance Sheet and Accounts. December 31st 1955

FINANCIAL REPORT OF THE GOVERNING BODY

1. The Balance Sheet as at 31st December 1955 shows balances to the credit of the various funds as follows: Capital Fund £685,122; Specific Funds £137,184; Bequest Funds £18,825 and Contingency Reserve £27,194.

2. The General Fund Income and Expenditure Account shows the income for the year as £125,000 compared with £123,997 in 1954. Expenditure amounted to £141,841 against £124,678 last year. The deficit for the year is £16,841 compared with a deficit of £681 in 1954.

3. The year's deficit of £16,841 shown by the General Fund Income and Expenditure account has been written off against the Contingency Reserve.

4. Stocks of Sera, Vaccine Lymph and Horses on hand at December 31st have the nominal value of £9,864, £5,193 and £4,704 respectively.

5. MESSRS. COOPER BROTHERS & Co., the retiring Auditors will, subject to the provisions of the Companies' Act, 1948, be re-appointed.

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

CHELSEA BRIDGE ROAD,
LONDON, S.W. 1.

10th May, 1956.

BALANCE SHEET

(1954) £		£	£
	Capital Fund:—		
	Donations, &c., received to date from the following:—		
2,000	Dr. Ludwig Mond (1893)	2,000	
46,380	Borridge Trustees (1893/98)	46,380	
10,000	Worshipful Company of Grocers (1894)	10,000	
250,000	Lord Iveagh (1900)	250,000	
18,904	Lord Lister's Bequest (1913/23)	18,904	
7,114	William Henry Clarke Bequest (1923/6)	7,114	
3,400	Rockefeller Foundation (1935/6)	3,400	
22,669	Other Donations and Legacies (1891-1954)	22,669	
	General Fund Income and Expenditure Account Accumulated Surplus as at 31st December, 1954 .. 339,128		
339,128	*Less* Amounts written off and loss on sale of investments 14,473	324,655	
699,595			685,122
	Specific Funds:—		
93,990	Sinking Fund for Freehold Buildings 95,905		
36,114	Pension Fund 36,259		
5,020	Re-endowment Fund 5,020		
		137,184	
	Bequest Funds:—		
10,529	Jenner Memorial Studentship Fund 10,465		
8,138	Morna Macleod Scholarship Fund 8,360	18,825	
153,791			156,009
	Specific Grants and Legacies Unexpended:—		
772	Cancer Research Legacies (1937-50)	772	
2,048	Royal Society Grant (1951)	1,583	
4,393	Nuffield Foundation Grants (1952-5)	3,722	
2,000	Guinness Lister Research Grant (1953-5)	4,518	
9,213			10,595
	Contingency Reserve:—		
	As at 31st December 1954	44,035	
	Less Deficit on General Fund Income and Expenditure Account, 1955	16,841	
44,035			27,194
	Current Liabilities:—		
15,721	Creditors and accrued charges		21,806

PAUL FILDES, *Acting Chairman of Governing Body.*

WAVERLEY, *Hon. Treasurer.*

£922,355	£900,726

REPORT OF THE AUDITORS

We have examined the above Balance Sheet and annexed Income and Expenditure Account which are in all the information and explanations which we considered necessary for our audit. In our opinion these accounts information required by the Companies Act, 1948, and show a true and fair view of the state of the Institute's

London, 17th May, 1956.

31st DECEMBER 1955.

(1954) £		£	£	£
	Fixed Assets :—			
	FREEHOLD PROPERTY at cost :			
73,548	Land and Buildings, Chelsea	73,548		
20,456	Queensberry Lodge Estate, Elstree	20,456		
2,049	House, Bushey	2,049		
			96,053	
	(*Note : Additions and replacements since 1912 at Elstree and 1935 at Chelsea have been charged to Revenue*).			
	FURNITURE, FITTINGS, SCIENTIFIC APPARATUS AND BOOKS :—			
2,472	At cost *less* depreciation to 31st December 1920		2,472	
98,525	(*Note : Additions and replacements since 31st December, 1920 have been charged to Revenue*)			98,525
	General, Specific and Bequest Funds.			
	Quoted Investments at cost, less amounts written off and Uninvested Cash :—			
		Investments	Cash	
607,532	GENERAL	606,421	—	606,421
	SPECIFIC :			
93,990	Sinking Fund for Freehold Buildings ..	91,705	4,200	95,905
36,114	Pension Fund	35,543	716	36,259
5,020	Re-endowment Fund	4,941	79	5,020
	BEQUEST :			
10,529	Jenner Memorial Studentship Fund ..	8,545	1,920	10,465
8,138	Morna Macleod Scholarship Fund ..	7,606	754	8,360
761,323		754,761	7,669	762,430	762,430
	(*Market Value £774,425*)			
	Current Assets :—			
57,360	Debtors and Payments in advance		27,003	
2,187	Bills Receivable		2,161	
2,960	Balance at Bankers and Cash in hand		10,607	
62,507				39,771
	(*Notes : See paragraph 4 Governing Body's Financial Report for nominal values of Sera, Vaccine Lymph and Horses which have not been brought into the accounts.*			
	There is a contingent liability of £22,950 in respect of investments not fully called up).			
£922,355				£900,726

TO THE MEMBERS.

agreement with the books of account. In our opinion proper books of account have been kept. We have obtained amplified by the information given in paragraph 4 of the Financial Report of the Governing Body give the affairs at 31st December, 1955, and of the deficit for the year ended on that date.

COOPER BROTHERS & CO.
Chartered Accountants

INCOME AND EXPENDITURE ACCOUNTS

General

(1954) £		*Total Expenditure* £	*External Contributions* £	£
52,493	Salaries and Wages	93,258	36,677	56,581
5,632	Emoluments of two members of the Governing Body in an Executive Capacity	6,471	—	6,471
1,973	Premiums on Federated Superannuation Policies	3,484	966	2,518
3,104	Premium on Group Pension Policy	3,249	178	3,071
3,288	Rent, Rates and Insurance	3,952	305	3,647
8,551	Gas, Water, Fuel and Electricity	12,042	2,386	9,656
1,311	Office Expenses, Stationery and Printing ...	2,041	238	1,803
263	Auditors' Fee	210	—	210
652	Travelling Expenses	1,587	195	1,392
1,286	Biochemistry Expenses	3,387	1,957	1,430
1,104	Microbiology, Immunology and Experimental Pathology Expenses	2,751	1,607	1,144
501	Biophysics Expenses	907	472	435
—	Virology Expenses	2,128	—	2,128
10,350	Serum, Vaccine and Vaccine Lymph Expenses	16,999	1,456	15,543
6,913	Animals	6,958	1 790	5,168
7,404	Animal House Expenses and Forage	9,380	965	8,415
13,314	Buildings, Alterations, Repairs and Renewals ...	16,050	518	15,532
419	General Apparatus and New Installations ...	620	—	620
903	Library Expenses	912	—	912
1,083	General Stores	931	—	931
699	Staff Canteen Loss	753	170	583
—	Blood Products Laboratory Expenses	2,213	2,213	—
3,435	Amount transferred to Sinking Fund for Freehold Buildings (including £3,227 Interest on Investments)	3,651	—	3,651
£124,678		£193,984	£52,093	£141,841

Pension Fund.

(1954) £		£	(1954) £		£
1,600	Pensions	1,461	1,606	Interest on Investments (gross) ...	1,606
6	Balance added to Fund ...	145			
£1,606		£1,606	£1,606		£1,606

Jenner Memorial Studentship Fund.

£		£	£		£
51	Stipend of Student	354	290	Interest on Investments (gross) ...	290
239	Balance added to Fund	—	—	Balance deducted from Fund ...	64
£290		£354	£290		£354

Morna Macleod Scholarship Fund.

£		£	£		£
89	Stipend of Student	—	227	Interest on Investments (gross) ...	222
213	Balance added to Fund	222	75	Post-War Credits	—
£302		£222	£302		£222

for the year ended 31st December 1955.

Fund.

(1954) £		£	£
	Interest and Dividends on Investments:		
25,940	General Fund	27,794	
3,011	Sinking Fund	3,227	
			31,021
86,404	Sales of Sera, Vaccines, Vaccine Lymph, &c.		88,767
8,642	Rent		5,212
	Deficit transferred to Contingency Reserve after charging to Expenditure		
681	£14,644 for additions to property and equipment		16,841
£124,678			£141,841

Guinness - Lister Research Grant.

(1954) £		£	(1954) £		£
5,291	Salaries and Wages	5,479	111	Balance at 1st January, 1955...	2,000
2,820	Laboratory Expenses	2,004	10,000	Amount received	10,000
2,000	Balance carried forward ...	4,517			
£10,111		£12,000	£10,111		£12,000

Nuffield Foundation Grants.

(1954) £		£	(1954) £		£
6,413	Salaries, Wages, Laboratory Expenses and Animals	6,671	3,806	Balance at 1st January, 1955...	4,393
4,393	Balance carried forward ...	3,722	7,000	Amounts received	6,000
£10,806		£10,393	£10,806		£10,393

INVESTMENTS AT 31st DECEMBER 1955.

GENERAL FUND.

		Balance Sheet Value		Market Value
£10,000	A.P.V. Co., Ltd., 5 per cent. First Mortgage Deb. Stock, 1980/85 ..	£9,664	..	£9,350
800	Albright & Wilson Ltd., Old Ordinary Stock Units of 5/-	841	..	840
5,200	,, ,, New Ordinary Stock Units of 5/- ..	4,926	..	5,460
£5,000	Allied Bakeries Ltd., 5 per cent. Unsecured Loan Stock, 1960/70 ..	4,819	..	4,775
£2,900	Australia, Commonwealth of, 4½ per cent. Registered Stock, 1960/62	2,666	..	2,827
£12,000	Australia, Commonwealth of, 3 per cent. Registered Stock, 1972/74	12,121	..	9,060
£4,000	Bankers Investment Trust Ltd., Deferred Stock	7,806	..	12,200
£2,000	British Electricity 3 per cent. Guaranteed Stock, 1974/77.. ..	1,898	..	1,590
£15,000	,, ,, 3½ ,, ,, ,, 1976/79.. ..	14,925	..	12,525
£4,505	British Gas 3 per cent. Guaranteed Stock, 1990/95	3,638	..	3,356
2,000	British Oxygen Co., Ltd., Ordinary Stock Units of £1	6,165	..	6,300
£10,000	British Titan Products Co., Ltd., 5½ per cent. Unsecured Loan Stock, 1970/75 (40 per cent. paid)	4,000	..	3,900
£20,000	British Transport 3 per cent. Guaranteed Stock, 1967/72	20,259	..	15,000
£55,496	,, ,, ,, ,, ,, 1978/88	55,496	..	40,789
3,500	Cater Brightwen & Co., Ltd., Ordinary Stock Units of £1.. ..	10,872	..	9,537
£20,000	4 per cent. Consolidated Loan Stock, 1957, or after	18,568	..	16,900
£13,000	3½ per cent. Conversion Loan Stock, 1961, or after	12,974	..	9,945
3,250	Debenture & Capital Investment Trust Ltd., Ordinary Stock Units of £1	6,586	..	13,812
4,000	Dorman Long & Co , Ltd., Ordinary Shares of £1	4,981	..	6,550
125	Enfield Rolling Mills Ltd., Ordinary Stock Units of £1	310	..	473
~~£32,000~~	~~4 per cent. Funding Loan, 1960/90~~	25,995	..	29,600
£1,125	General Consolidated Investment Trust Ltd., Ordinary Stock ..	2,236	..	3,881
300	Hadfields Ltd., Ordinary Shares of £1	393	..	435
200	Harrods Ltd., Ordinary Stock Units of £1	443	..	537
£10,000	Hope & Anchor Breweries Ltd., 5½ per cent. Mortgage Debenture Stock, 1980/85	9,833	..	10,000
£3,000	Kenya Power Co., Ltd., 5½ per cent. Debenture Stock, 1975/85 (50 per cent. paid)	2,429	..	2,175
£10,000	Kraft Foods Ltd., 5 per cent. Debenture Stock 1965/75 (50 per cent. paid)	5,000	..	4,250
4,000	Lancashire Steel Corporation Ltd., Ordinary Shares of £1.. ..	5,328	..	8,000
500	Laporte Industries Ltd., Ordinary Shares of 5/-	347	..	456
£10,000	R. A. Lister Ltd., 5 per cent. Unsecured Loan Stock, 1960/65 ..	9,975	..	9,475
£3,750	London & Montrose Investment Trust Ltd., Ordinary Stock ..	7,893	..	17,437
£3,125	London Scottish American Trust Ltd., Deferred Stock	5,942	..	10,781
£1,650	London Trust Co., Ltd., Deferred Stock	3,604	..	7,012
£1,375	Lowland Investment Co. Ltd., Ordinary Stock	2,683	..	4,425
22,500	Mercantile Investment & General Trust Co. Ltd., Ordinary Stock Units of 5/-	13,401	..	22,219
£25,000	New Zealand 3½ per cent. Stock, 1962/65	21,989	..	21 875
£10,000	Norvic Shoe Co., Ltd., 5 per cent. Unsecured Loan Stock, 1970/75 ..	9,800	..	9,650
£10,000	Peninsular & Oriental Steam Navigation Co., 5 per cent. Debenture Stock, 1975/80 (50 per cent. paid)	4,842	..	5,300
£3,000	Port of London Authority—Port of London 3½ per cent. Registered Stock, 1965/75	2,687	..	2,385
20,000	Rio Claro Investment Trust Ltd., Ordinary Stock Units of 5/- ..	11,192	..	19,000
20,000	River Plate & General Investment Trust Co., Ltd., Deferred Stock Units of 5/-	7,691	..	12,000
£25,000	3 per cent. Savings Bonds 1955/65	25,000	..	22,125
£66,300	,, ,, ,, 1960/70	66,417	..	54,034
£38,300	,, ,, ,, 1965/75	33,857	..	30,448
£26,100	South Australian Government 3 per cent. Consolidated Stock, 1916 or after	16,800	..	16,834
5,250	Sphere Investment Trust Ltd., Ordinary Shares of £1	7,830	..	14,497
10,182	Standard Trust Ltd., Ordinary Stock Units of 5/-	3,674	..	8,018
150	The Steetley Co., Ltd., New Ordinary Shares of £1	250	..	422
£7,500	Sterling Trust Ltd., Ordinary Stock	8,731	..	17,625
£6,750	Third Guardian Trust Ltd., Ordinary Stock	8,009	..	13,162
£10,000	United Gas Industries Ltd., 6 per cent. Unsecured Loan Stock, 1973/75 (50 per cent. paid)	5,000	..	5,100
£9,000	United States Debenture Corporation Ltd., Ordinary Stock ..	12,553	..	18,450
£50,000	3½ War Loan, 1952, or after	49,537	..	38,250
£6,000	Witan Investment Co. Ltd., Ordinary Stock	11,145	..	14,100
		£606,421		£639,087

SINKING FUND FOR FREEHOLD BUILDINGS.

		Balance Sheet Value	Market Value
£6,400	British Electricity 3 per cent. Guaranteed Stock, 1974/77	£6,260	£5,088
£3,000	,, ,, 3 ,, ,, ,, 1968/73	2,916	2,415
£16,500	3½ per cent. Conversion Loan Stock, 1961 or after	15,018	12,622
£10,200	4 per cent. Funding Loan, 1960/90	9,079	9,435
£4,500	3 ,, ,, ,, 1959/69	3,876	3,712
£2,000	2½ per cent. National War Bonds, 1954/56	2,106	1,980
£3,500	3 per cent. Savings Bonds, 1955/65	3,518	3,097
£10,000	,, ,, ,, 1960/70	9,622	8,150
£31,600	,, ,, ,, 1965/75	31,600	25,122
£3,000	Third Guardian Trust Ltd., Ordinary Stock	2,722	5,850
2,000	Union Discount Co. of London Ltd., Stock Units of £1	4,988	4,800
		£91,705	£82,271

PENSION FUND.

£22,000	4 per cent. Funding Loan, 1960/90	£17,165	£20,350
£18,000	3½ per cent. Conversion Loan Stock, 1961 or after	15,173	13,770
£2,200	3 per cent. Savings Bonds, 1960/70	2,205	1,793
£1,000	3 ,, ,, ,, 1965/75	1,000	795
		£35,543	£36,708

JENNER MEMORIAL STUDENTSHIP FUND.

£2,800	4 per cent. Funding Loan, 1960/90	£2,705	£2,590
£1,986	British Transport 3 per cent. Guaranteed Stock, 1978/88 ..	1,986	1,460
£2,650	Southwark & Vauxhall Water Co. 3 per cent. "B" Debentures ..	2,757	1,683
£1,300	Liverpool Corporation 3 per cent. Stock, 1942, or after ..	1,097	825
		£8,545	£6,558

MORNA MACLEOD SCHOLARSHIP FUND.

£1,000	3½ per cent. Defence Bonds, Conversion Issue	£1,000	£1,000
£500	3 per cent. Savings Bonds, 1960/70	500	408
£5,800	2½ per cent. Treasury Stock, 1975 or after	5,203	3,277
£900	British Electricity 3 per cent. Guaranteed Stock, 1974/77 ..	903	715
		£7,606	£5,400

RE-ENDOWMENT FUND.

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THE LISTER INSTITUTE
OF
PREVENTIVE MEDICINE

REPORT
OF THE
GOVERNING BODY
1956

CHELSEA BRIDGE ROAD, LONDON, S.W.1

THE GOVERNING BODY

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ANNUAL GENERAL MEETING

OF

The Lister Institute of Preventive Medicine

June 21st. 1956

REPORT OF THE GOVERNING BODY

The Governing Body has the honour to present its report on the work of the Institute for the year 1955/56.

GOVERNING BODY

At its last meeting the Council re-elected Sir Henry Dale, Sir Paul Fildes and Sir Wilson Jameson as its representatives on the Governing Body. Dr. D. McClean was re-elected as the Scientific Staff's representative.

COUNCIL

At last year's Annual General Meeting the three retiring members of the Council, Dr. G. S. Wilson, Sir Merrik Burrell and Sir Wilson Jameson, were re-elected. Professor G. L. Brown was also elected to the Council as a representative of the Members.

The three members of Council who are due to retire this year in accordance with the Articles of Association, but are eligible for re-election, are Professor A. V. Hill, Sir Alan Drury and Dame Harriette Chick, each a representative of the members of the Institute.

MEMBERS

The Governing Body records with regret the deaths during the year of Professor P. A. Buxton, Dr. A. Felix, Lord Horder, Professor T. J. Mackie and Professor J. M. Turnbull. Dr. Felix was a member of the Institute staff for a number of years before the war and since his retirement from the Public Health Laboratory Service had again been working at the Institute.

STAFF

Dr. W. J. Whelan, Dr. Winifred Watkins and Dr. W. C. Crimmin were appointed to the Biochemistry department, Dr. Elizabeth Sparrow to the department of Experimental Pathology, Miss L. R. Thomas to the Smallpox Vaccine department, Mr. M. Garay to the Bacterial Vaccines department and Mr. R. H. Painter to the Blood Products Laboratory and Mr. W. Blyth and Miss M. Beech to the unit for research in non-specific urethritis.

Miss J. Mattingley, Dr. G. Owen, Miss D. Thow and Miss M. Beech resigned during the year.

Mrs. Helen Bernstein, Mme. E. de Margerie, and Mr. A. M. Porter, of the laboratories of Arthur Guinness Son & Co. Ltd., joined the Guinness-Lister Unit.

Visitors. The following visitors worked for short periods in the Institute laboratories: Dr. F. Bozok, Turkish Red Crescent, Ankara; Dr. Mir Chasmi, Institute Rayzi, Iran; Dr. J. Crookston, Canadian Travelling Scholarship; Mr. S. Davidovici, Israeli Institute for Biological Research, New Ziona, Israel; Dr. Marjorie Krauss, New York University, U.S.A.; Drs. B. Maupin, H. Perrot and F. Henaff, Etablissement Central de Reanimation-Transfusion de l'Armee, Clamart, France; Dr. S. G. Pavlidis, Institute of Hygiene, Athens; Dr. K. Porchinski, Serotherapeutic Institute, Vienna, Austria; Dr. F. Potsch, Director, Public Health Laboratory, Klagenfurt, Austria; Dr. G. Prodi, Instituto di Patologia Generale, Universita di Bologna; Miss A. M. Scott, Laboratory Service H.Q., Yaba, Nigeria; Dr. A. W. Shaafsma, South African Institute for Medical Research, Johannesburg.

Staff Visits. At the invitation of the Council for International Organisations of Medical Sciences, Professor A. A. Miles took part in a symposium on "The Physiopathology of the Reticulo-endothelial System" held in Paris, July, 1955, and at the invitation of the New York Academy of Sciences took part in a conference on "Natural Resistance to Infection" in New York, March, 1956.

Dr. W. d'A. Maycock attended the 1st European Meeting of Biological Standardisation organised by the International Association of the Societies of Microbiology held in Lyon, June, 1955; and visited the National Research Council in Washington, U.S.A., in August, 1955, on behalf of the Medical Research Council, in connection with the Anglo-American Dextran Trial.

Dr. D. McClean visited the State Bacteriological Laboratory, Stockholm, to study the technique of preparing smallpox vaccine by tissue culture in bovine or sheep embryo. In November, 1955, Mr. Standfast visited various medical centres in Yugoslavia as consultant on behalf of the World Health Organisation, in connection with studies of whooping cough and typhoid immunization.

Dr. L. H. Collier paid a three months' visit to various virus research laboratories in the U.S.A. and visited clinics and laboratories in Morocco, Tunisia and Egypt as a consultant on behalf of the World Health Organisation Trachoma Project. Dr. J. M. Horton spent three months at the State Serum Institute, Copenhagen, studying the serology of *B. pertussis*.

The Governing Body notes with satisfaction the successful continuance of the researches under Professor Miles and Professor Morgan, made possible by the generous benefaction of the Nuffield Foundation.

The Blood Group Research Unit and the Blood Group Reference Laboratories are still accommodated at the Institute, and Miss E. M. Hume continues to edit Nutrition Abstracts and Reviews on behalf of the Medical Research Council and the Commonwealth Bureau of Animal Nutrition, Aberdeen.

MICROBIOLOGY

Protozoology

Antigenic Structure of Trichomonas. Dr. Muriel Robertson has continued her antigenic analysis of the two serological varieties of the protozoon *Trichomonas fœtus* by the Ouchterlony precipitin technique in agar gels; at least five recognisable antigenic components are present in Trichomonas. Antigen fractions of various species of Tetrahymena, and of single strains and mating types of these ciliates grown under different conditions are also being analysed by gel-diffusion methods.

Cytology of Amœbo-flagellates. Mr. Pittam is surveying the free-living protozoa in pond and ditch water with a view to their cultivation for detailed study. He is investigating the cytology and inheritance of the flagellar apparatus in the Dimastigamœbidæ (forms exhibiting alternating amœboid and flagellate phases in their life cycle). The small, actively motile soil amœba, *Nægleria gruberi*, which is the most accessible species in this family, has been established in artificial culture with the bacterium *Aerobacter aerogenes* as a food source; and is being acclimatized to growth on bacteria-free media.

Whooping Cough Bacillus

Mr. Standfast and Dr. Horton have continued their work on the characterization of the immunizing antigens of *Bordetella pertussis* (*Hæmophilus pertussis*), the mechanism of their action, and the factors determining the virulence of this organism for laboratory animals.

Assay of Protective Antigen. There is little doubt that the "Intracerebral Mouse Test" for the potency of whooping cough vaccines is a valid test but large numbers of mice are needed to obtain significant results; and although it is practicable with vaccines for human use, it is cumbersome and expensive for large numbers of experimental vaccines, cell fractions, etc. Extensive investigations, however, have not led to an *in vitro* test for the protective antigen that would replace the mouse test. Thus by Ouchterlony precipitin technique in agar gels, at least 17 distinct and reproducible lines occur with pertussis extracts, but none could be identified as those of protective antigen. Nor was the chief line of Pillemer's "PA" fraction found in

certain potent vaccines, which suggests that if the protective antigen gives a line, chemical purification may have changed it sufficiently to alter its line. Neither red cell agglutination nor the complement lysis test are suitable, though there are indications that these tests may be made so.

With Dr. Thow further investigations were made of the 'Sublethal Intranasal Test', which confirm the view that the antigens and antibodies in this test are different from those concerned in the intracerebral test.

Distinction of Protective Antigen and Other Antigens. (a) Agglutinogen. Protective antibody remains in pertussis antiserum after the absorption of the agglutinins by *B. pertussis* suspensions (1953 Report). This work has been repeated with suspensions of the four main serological types of *B pertussis* described by Krag Andersen, with the same result, confirming the distinction of agglutinin and protective antibody.

Distinction of Protective Antigen and Other Antigens. (b) Histamine-Sensitizing Factor. The histamine-sensitizing antigen (HSF) has been investigated by Dr. Horton in the hope that histamine-sensitizing potency in the mouse would parallel protective potency. Two fractions of the bacillus were obtained, with very different ratios of histamine sensitizing to protective dose. This result supports the view of Pittman in America, based on the fact that the HSF and protective antigens deteriorate at different rates in stored vaccines, that the two substances are not identical.

Growth Factors for B. pertussis. Dr. Rowatt completed a survey of amino acid metabolism of the genus *Bordetella.* During growth of each of the three species in a liquid medium, glutamic acid was metabolized before any other amino acid. Growth of *B. pertussis* was proportional to the quantity of glutamic acid, and other amino acids were used in quantity only when glutamate remained. Two other factors were found to be necessary for growth of *B. pertussis* in a semi-synthetic medium : one of these increases the rate of growth and, in a medium poor in this factor, small inocula die out after a few generations, before growth has become visible. The factor, which is present in small concentrations in acid digests of casein and in high concentrations in red blood cells, is probably not a common amino acid. Commercial hæmin has some activity but itself does not appear to be the active substance.

The second factor occurs in casein digest but it affects the amount of growth rather than its rate. It occurs in yeast, and to a small extent in blood.

Typhoid Bacillus

Assay of Protective Antigens. Mr. Standfast and Dr. Horton continued the investigation of *in vivo* and *in vitro* laboratory assays of the potency of *Salmonella typhi* vaccines, as part of a collaborative study initiated by the World Health Organisation.

Vole Bacillus

Miss Card has continued her investigation of *Mycobacterium* var. *muris.*

Vaccines from solid and liquid medium. Vaccines prepared in liquid media have been compared by *in vitro* and *in vivo* tests with vaccines prepared on the routine solid medium. Little difference was found between the two types of vaccine, except that the liquid-grown vaccines were better dispersed and produced larger lesions in the skin of guinea-pigs. This increase in lesion size may be due to some constituent of the medium.

Amino acid Metabolism. For the preparation of the semi-synthetic liquid medium an investigation was made of the amino acid metabolism of the vole bacillus. Asparagine, an amino acid commonly used for *Mycobacterium tuberculosis,* induces a pronounced lag in growth of the vole bacillus and is converted to aspartic and glutamic acids, the latter appearing to be the most important amino acid for the vole bacillus. Growth with glutamic acid is more granular than that with the amino acid mixture, unless glycine is present. .

Freeze-dried Vaccines. Freeze drying was investigated as a method of vaccine production. There is a progressive drop in viable count during the first few hours of the drying process, after which the count remains more or less stationary. Reconstitution of completely dried material produced some clumping and granular suspensions, so that the drop in viable count may be due to clumping and not to killing. This change in the dispersibility of the organisms occurs by the time gross drying is complete.

"Cording" has been observed in cultures grown in liquid medium containing an optimal quantity of a β-globulin fraction of serum.

Inheritance in Bacteria

Inheritance of Flagellar Characters and of Flagella. Dr. Stocker has continued his work on the "abortive transduction" of motility to non-motile *Salmonella* strains by bacteriophage and has confirmed the hypothesis (Report, 1955) that in this phenomenon a bacteriophage particle imports a fragment of bacterial genetic material into a non-motile cell, which in consequence becomes motile, and that the imported material never divides, but at each generation passes unaltered to one of the descendants. This explanation applies to several strains of Salmonella bacilli that are non-motile because they lack flagella, and to one "paralysed" strain, whose cells have flagella and yet are non-motile.

With Mme. de Margerie, he is studying abortive transduction in a non-motile strain in which, it is believed, the gene causing absence of flagella is linked to one determining the antigenic character of the flagella when present. The antigen present in the flagella of a single cell can be identified microscopically by the immobilising action of homologous anti-flagellar serum. Serum reacting with the antigen determined by the latent antigen-gene of this non-motile strain immobilises nearly all motile cells resulting from abortive transduction; so also does serum reacting only with the antigen of the "donor" strain on which the transducing phage was grown. It is inferred that these motile cells produce both these flagellar antigens, although they are never found together in normal cells; and that the phage-imported genetic material consists of a fragment of bacterial "chromosome" containing at least two linked genes.

A new kind of "unstable motile" strain has been encountered, whose cells lose and regain the ability to manufacture flagella, apparently through "mutation" and "back-mutation" at very high rates, perhaps about 0.01 per cell per generation.

In some situations (abortive transduction, etc.), motility is transmitted by a cell to one or a few only of its descendants in a way suggesting that hypothetical motility-conferring particles in the cell were distributed amongst its descendants without increase in number; and that each particle was a flagellum, or something determining its production. Mr. Quadling, in experiments in which synthesis of flagella, but not growth, was arrested by altering the temperature of incubation, has confirmed this hypothesis by finding a good correlation between number of stainable flagella, and number of motility-conferring particles inferred from pedigree experiments.

Mr. Quadling has shown that after synthesis of flagella ceases the flagella of a dividing *Salmonella* cell do not all pass to one cell, but are distributed about equally amongst its two daughter cells. This observation is incompatible with some prevalent hypotheses about the mode of growth of the bacterial cell wall.

"Residual Variation" in Flagellar Characters. Mr. Quadling has continued his investigations of the spontaneous appearance of rare motile cells in non-motile bacterial strains; these cells are not mutants, since their progeny are, like the original culture, predominantly non-motile. In one strain "events" leading to the production of an average of two or three motile cells occur with a frequency of about 10^{-5} per cell per generation. The "event" seems to be a transient ability of a cell to synthetise locomotor apparatus, which renders it motile, and which is transmitted to some of its descendants. Cells with this transient ability differ neither in genetic constitution nor in environment from the rest of the culture. It is proposed to call this kind of variation, not attributable to either genetic or environmental differences, "residual variation". It presumably results from random fluctuations in, e.g., the number of molecules of some essential material in the cell.

Fertility Agents in E. coli. Mrs. Bernstein has investigated the fertility agent (F) concerned in the mating behaviour of the bacterium *Escherichia coli*. This factor can be transmitted by cell-to-cell contact, and makes its host (and its descendants) fertile. Mrs. Bernstein has prepared cultures of *E. coli* strain K12, some infected with the F agent intrinsic in that strain (F12), and some infected with the F agent from another strain (F3). The agents F3 and F12 are qualitatively similar with respect to the fertility they confer, but there are considerable differences in the

proportions and kinds of genetic classes among recombinants produced by matings that involve the two F agents.

Detection of Transformation in Single Pneumococcal Cells. Miss Kraus and Dr. Stocker devised methods for detecting by microscopy the first appearance, in a culture, of encapsulated pneumococci resulting from treatment of cells of a non-encapsulated strain with genetically active deoxyribonucleic acid extracted from an encapsulated strain. The proportion of cells genetically transformed to encapsulation was very low; but the positive results obtained proved that the methods were satisfactory.

Bacterial Physiology

Flagellar Motility. Dr. Stocker has found that the flagella of *Salmonella* cells may be removed without killing the bacilli by vigorous stirring in a "blender". In a suitable medium, the de-flagellated bacteria re-grow their flagella, and at the same time regain their motility. These experiments favour the hypothesis that bacterial motility is effected by movement of flagella, rather than the contrary one that flagella are a consequence of motility.

The cells of a strain of *Salmonella typhimurium* become almost completely non-motile when washed in water or saline solutions, but regain motility in about 45 seconds when broth is added. The paralysis can be reversed by certain amino-acids, including some D-amino acids, by albumin and by high concentrations of phosphate. The rapidity of the reversing action and the efficacy of proteins, whose molecules are too large to penetrate the cell wall, suggest that flagella, which may be regarded as naked bacterial muscle-fibres, can only function when certain molecular groups are present in the medium to which they are exposed.

Flagellar Structure. Mr. Porter and Dr. Stocker are preparing purified flagella from normal and paralysed strains of bacteria, for X-ray diffraction analysis, in the hope that diffraction differences might throw some light on the molecular mechanism of contractility.

Physiology of Sporulation. Mr. Porter has continued his work, begun elsewhere, on the minimal nutritional requirements for sporulation in some strains of *Bacillus* species. Certain amino-acids permit sporulation in a glucose-ammonium-salts medium that otherwise supports only growth without sporulation. The amino-acids probably prevent the development of an acid reaction in the medium. Experiments are in progress on the ability of the strains to metabolise these and other amino-acids.

Bacterial Growth and Division. Mr. Perret has investigated the relation between bacterial growth and bacterial division under various experimental conditions. In a bacterial culture growing at a constant rate there should at any instant be twice as many newly-formed bacteria as there are bacteria about to divide, and the intermediate stages should be present in amounts given by the equation :—

$$N = 1{\cdot}386\ e^{-0{\cdot}693t}$$

where t is cell age, expressed as a fraction of the mean generation time, and N is the fraction of cells of age t present in the culture.

Under the phase-contrast microscope, cells of *Escherichia coli* show a changing pattern of dark and light bands. Double-banding seems to indicate the approach of cell division, and from the proportion, P, of doubly-banded cells in a culture the average cell-age, t_1, at which double-banding appears, is given by

$$t_1 = 1 - \log_{10} (1 + P)/0{\cdot}301.$$

E. coli (strain K12) has been grown in the continuous culture apparatus (Report, 1955) at various constant generation times between 0·5 and 8·0 hours, with either glucose, oxygen or organic nitrogen sources as the limiting nutrient. Differential counts show that the proportion of doubly-banded cells falls from over 90% at the shortest generation time to less than 10% at the longest generation time. A sixteen-fold increase in generation time therefore gives only a two-fold increase in the time which elapses between the appearance of double bands and the completion of cell division. This may mean that division involves mainly a re-arrangement of material already accumulated in the cell, and, once initiated, proceeds at a rate almost independent of the chemical composition of the medium.

Experiments in ordinary batch cultures with glucose as the limiting nutrient support this hypothesis. Growth ceases when the glucose is exhausted; but cell division seems to continue for some time because the cell size of glucose-starved cells may finally be as little as one-eighth the volume of unstarved cells. It remains to be determined how much of the decrease in volume is due to shrinkage rather than cell division.

Organisms of the Pleuropneumonia Group

Morphology. The comparison of the morphology of the pleuropneumonia-like organisms (PPLO) with that of the L-forms of bacteria, carried out by Dr. Klieneberger-Nobel in collaboration with Mr. F. W. Cuckow and Mr. M. S. C. Birbeck of the Chester Beatty Institute, has been completed. The "minimal reproductive units" of the PPLO were shown by electron microscopy to constitute a uniform phase, having diameters of 100-150 mμ. L-forms, by contrast, are 250-300 mμ in diameter. A similar ratio of sizes is indicated by filtration tests; large numbers of PPLO reproductive units pass filters of 0·3–0·25 μ average pore diameter (APD), whereas L-forms pass only through pores of 0·6–0·5 μ and rarely through pores of 0·4 μ. This work confirms the distinction between the two types of organism postulated by Dr. Klieneberger-Nobel on physiological and other grounds.

Non-Specific Urethritis in Man. Dr. Klieneberger-Nobel, with the assistance of Miss Beech, has continued the investigation of the still unsolved ætiology of non-specific urethritis, undertaken on behalf of the U.S. Public Health Authority, in collaboration with Dr. G. W. Csonka of St. Mary's Hospital and Dr. J. K. Oates of the Whitechapel Clinic. The definition of a complex boiled blood medium enriched with human serum, yeast extract and staphylococcal metabolite, highly favourable to the growth of PPLO from the human genital tract, has made possible a survey of the incidence of these organisms in material from diseased and normal genital tracts. Specimens from over 180 patients with "non-specific" urethritis, gonorrhœa, various other pathological conditions of the genitals and from normal people have so far yielded over 50 strains of PPLO. The strains are uncommon in normal persons, in patients recovered from genital infections, and in those with various diseases unaccompanied by genital inflammation. They are found in about half the cases of non-specific urethritis and a quarter of the cases of acute gonorrhœa in the male, and in nearly all cases of acute gonorrhœa and non-gonococcal genital infection in the female. It is possible that infection with PPLO is commonly dormant in the female, flares up under certain conditions, and is transmitted venereally to the male.

Miss Beech examined more than 30 strains (28 human) of PPLO organisms by complement fixation test with antisera to human and non-human strains; all the human strains are antigenically similar and differ from rat, mouse, cattle or sheep strains. Complement fixtion tests with PPLO antigens of sera from patients and healthy people are in progress.

Mr. Blyth has established a number of tissue cultures with a view to testing the pathogenicity of the human PPLO strains, and for the investigation of a possible virus causation of non-specific urethritis.

VIROLOGY

Trachoma

In preparation for research into the virus ætiology of trachoma, undertaken in collaboration with the Institute of Ophthalmology team working at the Hospital of St. John in Jerusalem and with other centres in the Middle East and North Africa, Dr. Collier has established a number of tissue cultures. He has completed a survey of the trachoma research in Morocco, Tunisia and Egypt.

Vaccinia Virus

Irradiated Vaccines. The work recorded in recent Reports on the antigenicity of vaccinia virus inactivated by ultra-violet light is part of a larger investigation of the possibility of inactivating the virus without destroying its immunizing properties. It may prove possible to produce a vaccine of killed or inactivated virus that will confer at least a basal immunity against infection. If such a vaccine is not potent enough to confer complete protection it should confer

enough to mitigate the unpleasant symptoms and complications that sometimes follow primary inoculation with living virus.

Dr. Kaplan, Dr. McClean and Mr. Vallet continue their work with irradiated vaccines with a view to testing their protective activity in human volunteers.

In collaboration with Mr. Bowen of the Atomic Energy Research Establishment, Harwell, the influence of gamma radiation on the antigenicity and survival of vaccinia virus is being investigated. It is also intended to carry out similar investigations of the action on vaccinia of β-propiolactone, reported by U.S. workers to inactivate several other viruses without destroying their antigenicity.

Dried Smallpox Vaccine. During recent years there has been increasing interest in the production of dried smallpox vaccines which can resist the hazards of storage and transport in tropical temperatures and so facilitate vaccination programmes under conditions in which the preservation of ordinary vaccine lymph has always been a major difficulty.

The first stage of the combined laboratory and clinical trial of the stability of dried smallpox vaccines, sponsored by the World Health Organisation, has been completed. Information has been obtained on the resistance of these vaccines to storage at temperatures up to 45°C. for prolonged periods and on the correlation between potency titrations by various methods in the laboratory and the percentage of successful vaccinations in the field. Titration by pock counting on the chorio-allantois of the chick embryo has proved to be more accurate and reliable than the official method of titration on the rabbit skin, as a means of estimating a minimum potency above which a vaccine may be expected to give the highest possible number of successful "takes". The dried vaccines have proved to be far more resistant to storage at high temperatures than any vaccine lymph hitherto available and with the vaccine prepared by the Institute, even after storage for 18 months at 45°C., 100% "takes" in man were achieved. This investigation was carried out in co-operation with the Department of Bacteriology, Liverpool University, the Epidemiological Research Laboratory of the Public Health Laboratory Service and the Department of Hygiene and Research of the Royal Air Force. An investigation designed to confirm the high degree of protection afforded by these vaccines even after they have partly deteriorated is now in progress.

Vaccine Production in Tissue Culture. The bulk production of smallpox vaccine in cultures of bovine embryo skin is in routine use in Sweden. This is a major advance in vaccine production since the resulting vaccine is free from bacteria and from the products of tissue inflammation. Production is also economical. There is considerable scope for further research on the best methods of applying these techniques to vaccine production, and Dr. McClean, Dr. Caplan and Miss Thomas are studying this and similar methods of virus production.

Titration of Vaccinia Virus. Although the titration of vaccinia virus by pock counting on the chorio-allantois of the chick embryo is the most sensitive method at present available, an adequate statistical study of the method has not been published. Dr. Kaplan, with Dr. G. Belyavin of University College Hospital Medical School, have assessed the variability of the test and the conformity of the distributions of the pock counts obtained with those theoretically expected. This work is now being prepared for publication.

Titration of Anti-Vaccinial Sera. The investigation of titration methods for anti-vaccinial sera is continuing. The inhibition of pock formation on the chorio-allantois, although produced by low concentrations of antibody, appears to be less precise than methods of lower sensitivity such as the intracerebral inoculation of mice or the cutaneous method in rabbits.

Reproductive Cycle of Vaccinia Virus. Dr. Kaplan is investigating the multiplication of vaccinia virus in the chorio-allantois of the chick embryo in order to determine the time relations of the appearance of various antigens in the reproductive cycle of the virus. An intimate knowledge of the course of events in virus multiplication may supply information leading to effective chemotherapy.

Bacteriophages

Antibiotics Active Against Bacteriophages. Dr. and Mrs. Asheshov have continued their search for antibiotics active against viruses, using a variety of bacteriophages of different biological properties as representative viruses for the purpose of testing cultures of Actinomyces moulds for the presence of antibiotics, in the hope that substances active against bacterial viruses may prove to be active against animal viruses.

The study of a promising group of substances (rutilantins) produced by an actinomycete, A220, was continued and a still simpler method of processing them was worked out. Another group of moulds was found to produce antiphage substances apparently identical with those produced by A220. These proved to be identical in biological activity (range of antiphage activity, etc.) but different in their chemical behaviour. A strain of A855y was established as the best producer of antibiotic. Relatively large amounts of purified material from A220 and A855y, were prepared for trials in animal virus infections in three different laboratories.

A third group of moulds—A772, A803 and A827—produced antiphage substances closely related chemically to A220 and to A855y, but differing considerably in biological activity. In spite of the chemical similarity, a new processing technique proved to be necessary for their isolation.

Antiviral action. Dr. L. Hoyle, of Public Health Laboratory Service, Northampton, finds that the partly purified substances A220 and A855y, both significantly suppress influenza infection in chick embryo in doses of one-eighth or less of the toxic dose. Dr. E. Weston Hurst of the Virus Department, I.C.I., Blackley, tested the substances on Eastern Equine Encephalomyelitis in mice, and Dr. F. Fulton, of the London School of Hygiene and Tropical Medicine, on Semliki virus in tissue culture. Neither preparation had any action.

Mrs Asheshov is studying the mode of action of the A220 antiphage substance on two different bacterial viruses—the *E. coli* phage T2 and *V. choleræ* phage C. Results are far from complete at the moment, but certain facts have been established. The substance affects neither the free phage particles nor the adsorption of phage on to susceptible bacteria. In bacteria infected with cholera phage C, the production of active phage particles is inhibited in the presence of A220. There are indications that an adaptive enzyme system may be involved in the inhibition, but this has not yet been established.

Bacteriophage Typing. Until his death, Dr. Felix continued his work on the typing of typhoid and paratyphoid bacilli by bacteriophages; and the co-ordination of the collaborative investigation of theoretical and practical aspects of this problem, conducted by the International Committee for Enteric Phage Typing.

E. coli *Bacteriophage.* Dr. Stocker's work on a new host-range mutant in phage T1 active against *Escherichia coli* (Report, 1955) has not provided the hoped-for information on the factors determining bacterial susceptibility to invasion by bacteriophage; and the work has been discontinued.

IMMUNOLOGY AND SEROLOGY

Paralysis of Immune Response

By Protozoal Antigens in Calves. In collaboration with Dr. W. R. Kerr of the Ministry of Agriculture of Northern Ireland, Dr. Robertson has completed her study of the phenomenon of immune paralysis in young calves. The antibody response to the antigens of the protozoon *Trichomonas fœtus* normally expected in the adult animal was greatly diminished in animals that had received large doses of *T. fœtus* antigen in the first three weeks of life: this partial paralysis of the immune response has persisted in animals up to the age of 31 months.

By Enzymes and Serum Proteins in Rabbits. Dr. Cinader and Dr. Dubert measured the elimination of radio-iodinated human serum albumin and diazo-benzene sulphonic acid human albumin from the circulation of normal rabbits, rabbits immune to human serum albumin and rabbits whose response to human serum albumin had been impaired by the injection of large doses of this antigen soon after birth.

Antibody and Antigen

Distribution of Antibody in the Serum Proteins. Dr. Mackay has shown, by the titration of bacterial agglutinating antibody in mammalian sera fractionated by the method of Kekwick and Mackay, that the naturally occurring agglutinins to *Salmonella* bacilli are present in the gamma globulin fraction (G3) of human sera, but in the G2 fraction of the sera of sheep and some other animals, which contains predominantly a mixture of alpha and beta globulins. In collaboration with Dr. A. E. Pierce and Mr. E. J. H. Ford, of the Institute of Animal Physiology, Babraham, she has studied the distribution of artificially induced bacterial agglutinins in the sheep. The sera of sheep receiving six doses of a *Salmonella* vaccine did not change in electrophoretic pattern either during the course of immunization or for six months after it; and during this period the naturally occurring agglutinin was consistently in the alpha and beta fraction, and the induced "immune" agglutinin was present in this and in the gamma globulin fraction as well.

Ribonucleases and Specific Anti-Ribonuclease. Dr. Cinader undertook the study of the serology of the ribonuclease enzymes (Report, 1955) in order to determine how far specific antibody combines with the chemically active part of a biologically active antigen molecule, and how far with the inert part. Enzyme-anti-enzyme systems are peculiarly suitable for this study, because residual activity can be tested *in vitro*, whereas in the classical work on inhibition of biological activity of toxins, residual activity must be measured *in vivo*, where both toxin and antibody are subject to largely indeterminate metabolic change. .

With Mr. Pearce, he has established the molecular combining ratios of specific rabbit anti-ribonuclease antibody with ribonuclease A; it approaches 3·0 in antibody excess, is 1·75 at the equivalent point and is 1·4 in the region of antigen excess where the complex is partly soluble.

In antibody excess, at a molecular ratio of 3·0, the amount of residual activity depends on the molecular weight of the substance used to detect it; thus it is 2% of the initial activity with nucleic acid, and 19% with a specimen of cytidine cyclic phosphate prepared by Dr. G. Buchanan.

It has not been possible to differentiate between ribonuclease A and B by diffusion against antibody in agar (Ouchterlony) or by the inhibition of the agglutination with specific antisera of tanned sensitized red cells; there were some differences in the amounts of protein nitrogen precipitated in the antigen excess zone. By electrophoresis analysis in agar by the method of Williams and Grabar, ribonuclease A and B each proved to consist of two components.

A *p*-amino benzene sulphonic acid derivative of ribonuclease has been prepared by diazotisation and its enzymic activity and other properties determined in comparison with those of the native enzyme; by the nitrogen assay of precipitins, by diffusion against antibody in agar gels and by electrophoresis in agar gels. This forms part of a study of ribonuclease and its derivative as a model system for serological cross-reactions.

Serological Identification of Insect Blood Meals

Tsetse Flies. A comprehensive study of natural feeding habits of tsetse flies had been made by Mr. Weitz and Miss Lee-Jones; the work was done with the co-operation of the staff of the East African Tsetse and Trypanosomiasis Research and Reclamation Organisation and various field workers from other departments. The blood meals of about 2,000 flies caught in seventeen different localities in the Sudan, Uganda, Tanganyika, Kenya and Southern Rhodesia were identified. The results provide, for the first time, an objective view of the food preferences of tsetse flies in Eastern Africa. The technique of identification (the inhibition of agglutination of tanned and sensitized red blood cells by extracts of blood meals (Report, 1954, 1955)) has proved to be reliable, and specific even for distinguishing the blood of closely related animals. The species of tsetse studied were : *Glossina morsitans, swynnertoni, pallidipes, palpalis, brevipalpis, austeni* and *longipennis*. Each species of fly has characteristic feeding habits which in some instances may be due to differences in their habitat. Thus the riverine species *G. palpalis* feeds largely on reptiles, although in places it feeds also on birds and some of the mammals which come to drink at the water edge. The savannah species (*G. morsitans* and *G. swynnertoni*) are dependent on the warthog (*Phocochoerus aethiopicus*) for half their supply of food, a surprising result in view of the expectation that ruminants were the main source of food. Other mammals such as rhinoceros and elephant are commonly used by the flies, whereas monkeys, baboons and birds are not often used. *G. pallipides* feeds chiefly on bushbuck (*Tragelaphus scriptus*). In Zanzibar the main host of *G. austeni* was the bushpig (*Potamochoerus koirpotamus;* 88% of all the feeds), an interesting

finding because *G. austeni* is a crepuscular feeder and the bushpig a creature of nocturnal habits. A striking feature is that none of the tsetse flies fed on hartebeest (*Alcelaphus buselaphus*), topi (*Damaliscus korrigum*), wildebeest (*Gorgon taurinus*) or zebra (*Equus burchellii*); though in some localities the hartebeest and zebra were very numerous and apparently readily available to the flies. Similarly, impala (*Aepyceros melampus*), thought to be the main source of food, provided only 0·8% of the feeds of *G. morsitans*, although there were numerous large herds in one area. The influence on the numerical results of a possible bias in the sampling of the flies caught in the bush is under investigation. Further studies are being made on the digestion of the serum proteins by flies which have been fed on different hosts. The apparent popularity of the warthog as a food source, as against the hartebeest and zebra, may be explained by the results of this work. The understanding of feeding habits is of great importance to workers on the ecology of flies and on the transmission of trypanosomes from game to domestic animals or man.

Mosquitoes. About 80,000 identification tests have been made on mosquito stomach contents, chiefly on behalf of malaria control schemes.

Antitoxin Production

Refinement of Therapeutic Antitoxins. Dr. Dolby has continued his studies on the removal of inactive material from pepsin-refined antitoxic horse sera. Attempts to adsorb the impurities on various ion-exchange resins, on zinc hydroxide and on calcium phosphate were unsuccessful. Activated fullers' earths and aluminium hydroxide both remove nitrogenous material with minimal loss of antoxin; and are being tested in the large scale production of refined antisera.

Proteolytic Enzymes for Refining Antisera. Many preparations of the enzyme pepsin when acting on certain substrates, such as hæmoglobin, show a series of peaks of activity at different pHs. Two of the major peaks are at pH 1·8–2·4 and pH 3·0–3·5. Since the activity at pH 3·2 is used in refining antitoxic sera, Dr. Dolby has tried to separate from purified pepsin a fraction with activity at this pH alone. Paper electrophoresis, chromatography on calcium phosphate columns and fractionation with ammonium sulphate failed to separate the activities. By tests with the Ouchterlony precipitin technique in agar gels against antisera to purified and crystalline pepsins the pepsins appeared to be single antigens. Further attempts at fractionation both of pepsin and of papain, which is also active at pH 3–4, are in progress.

Serological Assay of Tetanus Antitoxins. The multiple zones of flocculation that occur when tetanus antitoxin is titrated against crude tetanus toxin makes this method unreliable for the *in vitro* assay of antitoxin. By fractionation of crude toxin, Mr. Rodican has obtained a toxic material that flocculates in a single zone. In tests of a large number of natural and refined antitoxins, the potencies estimated from the position of this zone corresponded closely with that estimated by *in vivo* tests in mice. With a few natural antitoxic sera, the correlation was poor, due presumably to the low avidity of these antitoxins.

Immunizing Power of Clostridial Toxins. By growth of various species of gas-gangrene and other toxigenic clostridial species in cellophan bags, Mr. Rodican obtained filtrates at least ten times more toxic than those from the orthodox liquid cultures in flasks. These more potent filtrates, however, were not correspondingly better stimuli of antitoxin production when injected into horses.

EXPERIMENTAL PATHOLOGY

Mechanisms of Inflammation

Dr. Wilhelm, Professor Miles, Mr. Mill, Dr. Elder and Miss Sparrow continued the research into the mechanism of inflammation, undertaken as a basis for the understanding of tissue defences against microbial invasion. It is as yet directed mainly to the investigation of endogenous factors that increase capillary permeability, particularly those present in mammalian sera.

Permeablity Factors in Mammalian Sera. The system of a rapidly activable permeability factor and a more slowly acting native inhibitor, discovered in the serum of the guinea-pig, appears to be relatively stable. It is not altered in X-irradiation sickness, by heavy cortisone dosage, or by active and passive anaphylactic shock.

A similar system is present in the serum of man, rabbit and rat, and it is reasonable to predict that in some form it will be found in all mammalian sera. The rabbit and rat were studied intensively because it is possible to test serum fractions intracutaneously in the species of origin, whereas human serum fractions, except for limited work with wheal and flare reaction in the skin of volunteers, must be tested in an alien rodent species. In most of the tests applied, the main permeability factor in each of these three species qualitatively resemble that of the guinea-pig, though they are less potent. It is associated with the alpha globulins in the rat, with both alpha- and beta-globulins in the rabbit and mainly with beta-globulins in man. All are active in all species of laboratory animals tested. Dr. Elder showed that, as in the guinea-pig, the permeability factor in man is activable by simple dilution of the serum, though the degree and time-course of activation differ. The low potency is partly a result of the inapplicability of the standard techniques of serum fractionation; Mr. Mill has devised a method of isolating a human permeability factor nearly as active as that of the guinea-pig. Dr. Wilhelm demonstrated that the same is true in the rat, but that in the rabbit the factor is not activable by dilution. There is also strong indirect evidence that human, rabbit and rat sera contain inhibitors of the permeability factor, but that they have not yet been isolated.

Although there is substantial indirect evidence that the permeability factor is enzymic, Mr. Mill has found no substrate with which to demonstrate an action *in vitro*: and *in vivo* tests by Dr. Wilhelm, to distinguish between a direct enzymic action and the activation of a tissue enzyme, were negative.

Other Pharmacological Properties of Sera. Dr. Sparrow is investigating the pharmacology of serum dilutions and fractions, using isolated preparations of mammalian heart and ileum from the homologous species.

Permeability Factors in Therapeutic Antitoxins. Impurities in the antitoxic products used for therapeutic or prophylactic treatment increase the permeability of blood capillares in the skin of rabbits and guinea-pigs, as indicated by a rapid local exudation of dye present in the animal's circulation. Mr. Rodican finds that the factor increasing permeability in rabbit capillaries is a complex substance closely associated with protein, but in part able to pass a cellophan membrane. It is precipitable by various protein precipitants and only partially heat labile. It is hoped to devise means of removing this factor from antitoxic preparations for human use.

Mechanism of Capillary Permeability. With Professor Miles, Dr. Wilhelm has completed a study of histological changes in capillary endothelium induced by various permeability factors. The take-up of circulating colloidal substances is not stimulated specifically by histamine, but can be elicited as readily by guinea-pig serum permeability factor. All the evidence indicates that the guinea-pig factor is not a histamine liberator.

Treatment of large veins with histamine or the serum factor does not induce morphological changes in the inter-endothelial cement.

Bacterial Toxins and Capillary Permeability. Dr. Elder and Professor Miles investigated the time-course of changes in capillary permeability in the skin of the guinea-pig induced by toxins of the three gas-gangrene bacilli, *Cl. welchii, Cl. œdematiens, Cl. septicum.* In each case the permeability factor proved to be the main lethal toxin of the bacillus, and the precision of the neutralization of the permeability effect by the corresponding antitoxin suggests that the method might be useful for a rapid assay of antitoxins. With *Cl. welchii* and *Cl. septicum* toxin, permeability is increased from about the 45th to the 200th minute. The permeability effect of *Cl. œdematiens* toxin appears after 4-5 hours and may last for three days or more.

Mechanisms of Infection and Defence

The Decisive Period in the Early Stage of Infection. With Dr. Burke, Professor Miles completed a survey in the guinea-pig of the degree to which local skin infections by a variety of pathogens could be modified by local inhibitors of defence reaction, by systemic shock, and by circulating antibiotics. In nearly all cases, the maximum development of the local lesion was unaffected by these modifiers when the lesions were 3-4 hours old, indicating that the events in

the first few hours were decisive in determining the course of infection. The destruction of the infecting microbe during the decisive period was estimated as varying from 90% to 99.9999%, according to the pathogen used.

Bacterial Infection in Relation to inflammation. Dr. Burke and Professor Miles surveyed the vascular changes in the skin during the first few hours of local intracutaneous infections of the guinea-pig by nine different pathogens. During the decisive period, when a large part of the inoculum appeared to be killed or otherwise removed, there is only an early, transient increase in capillary permeability and stickiness of the capillary endothelium. The classical tissue response of diapedesis of leucocytes, and substantial increase in permeability occurs later, is maximum at 3½ hours and declines by the fifth hour; and there is no thrombosis of the blood or lymphatic vessels during the whole of this period. The magnitude of the 3½-hour response bore a constant relation to the ultimate maximum size of the infective lesion, suggesting that the decisive period is a valid concept not only for the fate of the infecting microbe, but also for the fate of the infected tissues.

Filtering Power of Lymph Nodes. Dr. Burke made a preliminary survey of the capacity of the cervical lymph nodes of the guinea-pig to prevent microbes introduced into the lymphatic vessels of the ear from reaching the blood stream. The results with the spores of *Bacillus pumilus* indicated a substantial, but by no means complete, hold-up of the spores in the nodes, which could be increased by pre-treatment of the node with certain permeability factors.

The Course of Fatal Bacterial Infection. Dr. Stocker's experiments in collaboration with Dr. G. G. Meynell of the Postgraduate Medical School on the infective process in mouse *salmonellosis* have been concluded. Mice were inoculated with graded doses of mixtures of equal parts of two or three genetically recognizable variants of the same *Salmonella* strain, obtained by transduction. In mice dying from inocula just large enough to cause fatal infections, the bacterial population at necropsy consisted of very unequal numbers of the variants, sometimes only one being found; but mice dying from considerably larger inocula yielded all variants in about equal proportions. A mouse dying from an inoculum just sufficient to cause death appears to die as a result of the multiplication of only a very few, sometimes only one, of the inoculated bacteria, even though these may have numbered some millions of live bacteria. This was the result predicted by the hypothesis that each inoculated bacterium has a low probability of multiplying, to cause, or participate in, a fatal infection, the probability being independent of the number of bacteria inoculated.

Plasma Transfusion Substitutes

Metabolism of Dextran. Of the various plasma substitutes investigated since gum arabic solution was first used in 1917, none has been shown to possess all the theoretically desirable properties, though dextran probably has more than most. The dextran molecule is composed of glucose-units and is at least partly, possibly completely, metabolised in the body, but the pathway of metabolism is not known. Dr. Maycock and Miss Turner have continued the investigation of the fate of intravenously injected dextran. That the liver possibly plays a large part in the metabolism of dextran is indicated by the finding that after an intravenous injection of dextran, the amount in the liver increases rapidly, reaching a peak on the fourth to sixth day; at this time the concentration in the liver is from 10 to 12 times that in the rest of the animal and between 14% and 16% of the injected dose is found in the liver. The liver dextran concentration then falls at first steeply and then more slowly; at 21 days it is some 3-6 times that of the rest of the body. The concentration of dextran in the spleen does not rise above twice that in the rest of the animal. Attempts to demonstrate *in vivo* the degradation of dextran using slices or suspensions of various tissues have been unsuccessful.

No evidence has been found to suggest that, in an animal given a series of injections of dextran, it is cleared more rapidly from the blood stream or through the kidney after each successive injection.

Dextran infused in man has been associated on occasion with reactions of anaphylactic or allergic-type, and has been shown by Kabat to be antigenic under certain conditions in man, the antigenicity apparently being related to the molecular weight of the dextran. During the last year investigation of the antigenicity of dextran in animals has been renewed.

BIOCHEMISTRY

The Human Blood Group Substances

The Nature of the AB Substance. Substances possessing blood group A, B and H properties occur in a water-soluble form in the secretions and tissue fluids of 80% of individuals.. The secretions from group A persons show only A activity and those from group B only B activity whereas the secretions from persons belonging to group AB show both A and B activity. Professor Morgan and Dr. Watkins have investigated the nature of the product of the human blood group *A* and *B* genes in individuals belonging to group AB in an attempt to determine whether the secretions in these heterozygous individuals contain molecules which carry both A and B specific groupings, or whether they contain a mixture of molecules some of which carry A and others B specificity. The specific group substances in artificial mixtures of A and B substances and in the material obtained from AB individuals were precipitated with anti-A or anti-B precipitating sera; the specific activity of the original materials, the solutions remaining after removal of the precipitates and the redissolved precipitates were determined by agglutination inhibition tests.

The results indicated that in the tissue fluids and secretions of group AB secretors a large proportion, if not all, of the macromolecules with blood group specificity possess both A and B properties. In the heterozygote, therefore, the *A* and *B* genes appear to give rise to a molecular species different from that produced by either gene in the homozygous state; in this instance the allelic genes appear to collaborate in producing the gene product. These results are important for any biochemical approach to the structure of the AB substance and as an example of the interaction of allelic genes in man.

Microbial Enzymes Destroying Blood Group Substances. The high degree of specificity shown by enzymes makes them useful tools for the determination of chemical structure and the enzymic approach has been used in studies on the human blood group substances. Dr. Watkins used zone electrophoresis on a starch column to purify the enzymes obtained from the protozoan flagellate *T. fœtus* which destroy the serological activity of the human blood group substances. By this method almost complete separation of the enzymes which destroy the B and H substances was achieved. It has been found that H activity is developed concomitantly with the loss of B specificity when the B inactivating enzyme acts on B substance. This change indicates that basic structures similar to those responsible for the serological specificity of H substance exist in the molecules showing B activity but that in the intact molecules the structures are masked by the B specific groupings.

Dr. Crimmin has synthesized p-nitrophenol-α-galactoside and other synthetic substrates which are required in the enzyme studies of Dr. Watkins and has also undertaken the preparation of L-fucose from seaweed and N-acetylgalactosamine from sheep trachæ; both these sugars are of importance as components of the human blood group substances and are required in highly purified form for the synthesis of known disaccharide structures to serve as model substrates for enzymic and serological studies.

Analysis of Blood Group A Substance. An important method for studying the structure of polysaccarides of large molecular size is the controlled hydrolysis by dilute acid or alkali followed by identification of the units liberated. Dr. Côté and Professor Morgan are studying the partial hydrolysis products obtained from blood group A substance of human origin. The results of preliminary experiments have allowed them to determine the most suitable conditions for hydrolysis which will bring about the limited release of certain simple sugars and oligosaccharides The units have been identified, separated by paper and column chromatography, and the partial hydrolysis of a large preparation of highly purified blood group A substance is now being undertaken.

Structural studies on the blood group substances necessitate the quantitative estimation at each stage of the sugars known to be present in the molecules. Accurate estimation of any one sugar component, however, is not always possible when it is present together with other sugars and therefore Mr. Ruszkiewicz has elaborated a quantitative method for the determination of simple sugars in complex mixtures which involves their separation on paper chromatograms, the location of the sugars with methanolic phenol-red borate reagent, and their colorimetric

determination with an anthrone reagent after elution from the paper chromatogram. Mr. Ruszkiewicz has continued to study the oxidation of the blood group substances with periodate and is now able to determine the ratio of glucosamine to galactosamine in these materials and estimate quantitatively the amount of formaldehyde liberated during oxidation.

Enzymes Solubilizing Blood Group Substances. Several methods for the isolation and purification of the human blood group substances have been described but it has generally been found that extraction of the freeze-dried tissue fluids and secretion with cold 90% phenol is a procedure which will readily eliminate the major part of the protein impurities usually present in native secretions or fluids. Unfortunately, for a reason which is not clear, the macromolecular blood group complexes are by this treatment rendered partly insoluble in water and so far no satisfactory method which avoids extreme pH change or heating has been available for bringing these water-insoluble materials into solution. Professor Morgan and Mr. McLoughlin have recently found that these mucopolysaccharide materials can be readily made soluble at pH 7 and at room temperature by the action of the enzyme ficin. By this means certain native materials such as the contents of paramucinous cysts which are not normally soluble in water, and the water-soluble products produced during freeze-drying or phenol treatment of native secretions, can be solubilized and made available for immunochemical study. The underlying process which brings about the solution of these mucopolysaccharide materials is being studied.

Isolation of Cyst Mucopolysaccharides. Miss Lawton has isolated mucopolysaccharides which possess group specificity from thirty ovarian cysts. These studies are of particular value in demonstrating the great variation in the mucopolysaccharide content of these native fluids and have led to the production of relatively large quantities of these specific materials for detailed immunological and chemical studies.

Carbohydrate Studies

Dr. Whelan joined the Institute's staff in January and with Mrs. Walker began to study the mechanism of the action of starch metabolizing enzymes by the use of radioactive substrate molecules. Dr. Warsi and Dr. Whelan are investigating the mechanism of the oxidation of monosaccharides by periodate and undertaking certain structural studies in the polysaccharide field. Mr. Haq is studying, with Dr. Whelan, the controlled synthesis of glucose oligosaccharides.

Biochemistry of Bacterial Toxins

Clostridium welchii *Toxin.* The variation in virulence of different strains of the gas gangrene bacillus *Cl. welchii* has been correlated in general with the capacity of the strain to produce lecithinase (α-toxin), but it now appears that there can be a qualitative difference between lecithinases from different strains. Dr. Macfarlane and Dr. Dolby have examined the lecithinases from five strains of *Cl. welchii* differing substantially in virulence for guinea-pigs and found that the biological potency, i.e., the ratio of toxicity in mice to the enzymic activity *in vitro,* varied over a threefold range, although all the lecithinases were neutralised by *Cl. welchii* α-antitoxin. The result may partly explain inter-strain variations in virulence, and suggest that inter-strain variation in potency of bacterial toxins may be a general phenomenon, although it cannot readily be recognised unless the biochemical action of the toxin is known.

Phospholipids as Substrates for Toxins. A main difficulty in elucidating the biochemical action of toxins is that, although their biological action may be narrowed down to an attack on a particular histological component or physiological function of a tissue, knowledge of the chemical structure concerned is imperfect. For this reason Dr. Macfarlane, with the assistance of Mr. Gray, has examined methods of isolating acetalphospholipids, whose structure and function are not well characterised, for use as test substances for the *in vitro* action of toxins. Fractionation of phospholipids by adsorption chromatography on silicic acid proved to be satisfactory and is being used to obtain the pure acetal compounds. One fraction isolated is similar to the complex phosphatidic acid "cardiolipin" isolated by Pangborn, which is extensively used as the antigen in

routine Wasserman tests for syphilis; and the work in progress may clarify the constitution of this substance and possibly simplify its preparation. Cardiolipin has hitherto been mainly of interest to serologists as a tool in diagnosis, but as a phospholipid widespread in tissues and presumably also present in some micro-organisms the compound is of considerable biochemical interest.

BIOPHYSICS

Human Plasma Proteins

Fibrinogen: Heterogeneity of Purified Preparation. Mr. Caspary has continued the physico-chemical studies of purified human fibrinogen. Examination of preparations by the more delicate techniques of boundary spreading in the electrophoresis apparatus and the ultra-centrifuge indicate a slight heterogeneity in size distribution and also a slight degree of electro-chemical heterogeneity of the fibrinogen, which is considerably influenced by the ionic strength of the solvent used. Diffusion experiments with a modified schlieren optical method reveal boundary asymmetry, and the data obtained have been used to calculate the different average types of diffusion coefficient. Purified bovine fibrinogen is being studied in parallel experiments.

Purified fibrinogen preparations have also been studied by immunological methods. Rabbit antiserum to human fibrinogen reacts strongly with a β-globulin fraction and weakly with γ- and α-globulin by precipitin titrations. Precipitin reactions after diffusion and electrophoresis in agar confirmed the presence of trace contaminants in these preparations.

The Antihæmophilic Factor. The antihæmophilic factor used at present in human therapeutics is prepared from bovine or porcine serum. The advantages of using for this purpose homologous material from normal human plasma are obvious. Using the method developed by Dr. Wolf for the assay of human antihæmophilic factor, Dr. Kekwick and Dr. Wolf have been devising procedures for increasing the recovery of this factor during the fractionation of human plasma, and for obtaining preparations of high potency. Though some progress has been made, the pronounced lability of the factor is a considerable obstacle to advance, and much time has been spent in determining the environmental conditions responsible for the decay of biological activity.

The Activation of Fibrinolysin. It has been suggested by Mullerz and others that the action of streptokinase in converting plasminogen to plasmin is mediated by a proactivator. The proactivator is believed to interact stochiometrically with streptokinase to form an activator, which then converts plasminogen to plasmin. The evidence for this mechanism is predominantly indirect, and Dr. Mackay and Dr. Kekwick have made attempts to separate the proactivator and plasminogen individually from a human plasma fraction which on treatment with streptokinase produces active plasmin.

Proteins in Pathological Conditions. Sedimentation and diffusion measurements have been made on proteins prepared from pathological sera, and on a sample of Bence-Jones protein, in collaboration with Professor Martin.

Stability of Albumin. In collaboration with Professor Martin, Dr. Mackay has studied the effects of heat on purified human albumin. Heating a 6% solution of human albumin in 0·1M $NaHCO_3$ at pH 6·5 at 60° for 10 hours divided the single electrophoretic component of unheated albumin into two, one of which sediments more rapidly in the ultracentrifuge, though it does not increase the viscosity, or the osmotic pressure of the albumin. With lower degrees of heating (45-55°), the proportion of the second component increases with increase both of temperature and period of exposure, but at 60° the period of exposure has little influence. The effect of a number of amino acids on the heat stability of albumin was tested, and albumin heated with different amounts of acetyl tryptophan was examined by moving boundary electrophoresis, electrophoresis on paper, and in the ultracentrifuge. The addition of 20 mg. acetyl-tryptophan per gram protein protects albumin from the effects of 10 hours at 60°, without any change in the electrophoretic or ultracentrifugal pattern.

Animal Serum Proteins

Serum Globulins in Young Rats. In collaboration with Professor F. W. Rogers Brambell and Dr. R. Halliday of the University College of N. Wales, Dr. Kekwick is studying the changes in the protein constitution of rat serum with age, from 10 days after birth until the rat becomes adult. In the rat the gut is permeable to proteins in milk and to others given by mouth until about the 20th day after birth, when an abrupt loss of permeability occurs. Concomitantly from 18 to 24 days a rapid fall in the gamma globulin content of the serum occurs, the concentration at 24 days being about 15% of that at 18 days. A subsequent slow increase becomes evident about the 30th day after birth and a stable adult level of gamma globulin is probably reached soon after the 40th day.

BLOOD

Blood Products Laboratory

The past year has been occupied in installing equipment in the new laboratory, and building up staff. The remaining section of the laboratory at Chelsea was moved to Elstree during the year, and the preparation of all plasma fractions for the National Health Service was resumed and has gradually increased. The equipment, however, is not complete and the laboratory is not yet ready to work at full capacity.

Stabilizers of Serum Albumin. Mr. Vallet has examined the use of sodium caprylate as a stabilizer for human albumin solutions during heating. With this agent pure albumin solutions can be heated at 60°C. for 10 hours without the formation of slow-moving components, which are found when acetyltryptophane is used as a stabilizer.

Blood Group Research Unit

The Unit continues to look for "new" blood groups and to study their inheritance: that is to search for tools which later may be of use in wider genetical, physiological, medical or anthropological investigations. There seems to be no sign of a limit to the number of "new" antigens to be discovered; and this is a good thing, for blood groups are still far and away the best characters available for the study of human genes and chromosomes. The discovery of a new blood group system means that one more recognizable point is fixed somewhere on the chromosomes, and other genes in its neighbourhood are thereupon exposed to detection. Most new antigens prove not to represent new systems, and therefore not fresh loci, but to represent new alleles at known loci. The more detectable alleles a genetic system has the more useful it is.

New antigens are most readily discovered in the study of antibodies formed by transfused people or by women who have had children suffering from hæmolytic disease of the new-born, and much of the Unit's time is taken in examining such sera. Most of the sera are sent by colleagues in the United States and each one represents the pick of thousands of other sera there tested and found to contain no antibody, or antibodies that presented no new problem. Many of those sera thought to contain "new" antibodies are found to contain mixtures of antibodies already known.

For the analysis of these highly selected immune antisera a large choice of red cells is needed of known antigenic combinations, which is kindly provided by members of the Institute, who give innumerable samples of their blood. From time to time samples from families are needed; some of these are provided by the families of colleagues and some by families of acquaintances living in a conveniently small area of Barnes. The other important need is a supply of routine but often very scarce antisera. For this the Unit is indebted to Dr. Mourant and the Blood Group Reference Laboratory.

The investigation of negro blood samples (Report, 1955) proved fruitful in increasing knowledge of three of the blood group systems in a way that no amount of work on white people could possibly have done.

The MNSs System in Negroes. The antigens S and s are part of the MN system of blood groups. In Europeans they are controlled by two allelic genes *S* and *s*, and all blood samples so far tested have contained the antigen S or s or both. In negroes, on the other hand, a small proportion lack both S *and* s. The most likely explanation is that such people are homozgous for a new allele S^u. Investigation of negro families supported this interpretation. There is no evidence that S^u exists in whites. This work was done in collaboration with Dr. T. J. Greenwalt of Milwaukee.

The Rh System in Negroes. A sample of serum from New York, sent by Dr. Cahan, was found to contain an antibody which at present is called anti-V. The corresponding antigen V has been found in the blood of: 40% of West Africans; 27% of New York negroes; 0·5% of New York whites (2 in 444); and 0·5% of English whites (2 in 407). The gene *V* is part of the Rh system; it has so far been found only in the chromosomes *cdef* and *cDef*. The precise place of *V* is not yet clear: it may be an allele of *f* or it may represent a new allelic site *G*. If *V* does prove to represent a new locus then the vast majority of Europeans must have a gene *g*, which could never have been suspected from a study of European blood alone.

The Duffy System in Negroes. In Europeans the Duffy system of blood groups consists of two antigens Fy^a and Fy^b, dependent on allelic genes Fy^a and Fy^b, and all blood samples so far tested have contained the antigen of Fy^a or Fy^b or both. A serum sent by Dr. Philip Levine, of New Jersey, proved to contain anti-Fy^b, of which there had previously been found only one example. As no negro samples had been tested with both antisera, the opportunity was taken to do so. Surprisingly, 68% of the samples reacted with neither antibody. Presumably in the negro there is a third allele which may be called *Fy*. If this interpretation is correct, then this is the biggest known single gene difference between negroes and whites. The gene frequencies are :—

	Whites	New York Negroes
Fy^a	41%	5%
Fy^b	59%	12%
Fy	0%	83%

The existence of the allele *Fy* could not have been detected by tests on white people.

These two phenotypes V+ and Fy(a–b–) are very powerful in telling whether a sample of blood is from a negro rather than from a white person. In New York 77% of samples from negroes would disclose their origin by being V+ or Fy(a–b–), and in West Africa over 90% would do so.

The P System in Whites. In 1926 Landsteiner and Levine discovered the P system of blood groups. In 1951 Levine and his colleagues discovered an antigen called Tj^a, possessed by practically everyone. So far only 14 people, members of eight families, have been found who lack the antigen. All these 14 people have the antibody anti-Tj^a in their serum. It is not a frankly immune antibody, like most blood group antibodies for it occurs regularly, like anti-A or anti-B. The antibody is said to be a very potent cause of early miscarriages. Recently the opportunity occurred of testing three samples of Tj(a–) blood. All were P–, which was very striking for only one in five white persons is expected to be P–. Following on this observation it was shown that Tj is not a system on its own, as it was thought to be, but part of the P system, which now appears as a complex system after thirty years of being apparently rather a dull and simple one. (The anti-Tj^a sera used in this investigation were kindly sent by colleagues in New York, Chicago, Johannesburg, Düsseldorf and Stockholm.)

For some years the Unit has been testing the blood of twins taking part in a psychiatric investigation undertaken by Dr. Eliot Slater and Mr. James Shields, of the Genetics Unit, the Maudsley Hospital. In collaboration with Dr. Sheila Callender of the Nuffield Department of Clinical Medicine, Oxford, the Unit has taken part in a large investigation of families in which pernicious anæmia occurs.

Blood Group Reference Laboratory

The Laboratory has continued to act primarily as the reference centre for blood-grouping problems for the United Kingdom, and under the auspices of the World Health Organisation as the world reference centre.

The routine demands on its services have continued their steady increase. This is true both of the supply of blood grouping sera to laboratories in the United Kingdom and abroad, and of tests carried out at the request of these laboratories. A number of laboratories have been helped to start their own services, by the supply of diagnostic sera and by the testing of the red cells of members of their staffs. In relation to clinical problems of transfusion and immunisation, and to the selection of grouping sera, large numbers of red cell and serum samples have been examined; in the identification of antibodies considerable use is now being made of enzyme-treated red cells, and of the preservation of rare antigenic red cell types by freezing with glycerol.

Dr. Parkin has investigated the antibody content, and the action upon red cells, of reconstituted small-pool dried human plasma, and has made an investigation into the reliability or otherwise of blood grouping by means of commercially-produced cards coated with dried serum.

The year has been a particularly active one in the field of anthropological blood group research, in charge of Miss Ikin. Tests have been performed on the blood of numerous tribes in East and West Africa, of the Walsers of Switzerland, of the Turks and the Arabic-speaking Eti-Turks, the Arabians, the Gurkhas from Nepal, the Burmese, the Veddahs of Ceylon and the Australian Aborigines.

Miss Ikin has also continued her work on a serum which specifically agglutinates red cells containing fœtal hæmoglobin.

In conclusion the Governing Body desires to record its great appreciation of the manner in which the scientific, administrative and technical staffs have worked together during the period under review, and to congratulate them on the interest and range of their scientific activities.

PAUL FILDES,

Acting Chairman.

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