THE HEALTH RESEARCH BOARD

Annual Report

and

Accounts 1989

An Bord Taighde Sláinte

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* Until November 1989
** Until June 1989

To the Minister for Health
In accordance with Section 22 of the Health Research Board (Establishment) Order, 1986 the Board herewith presents its Annual Report for the year ended 31st December, 1989.

CHAIRMAN'S STATEMENT

Professor M. X. FitzGerald

Chairman,
Health Research Board

The Health Research Board continues its strong commitment to a vigorous innovative programme of health research. Against a background of formidable funding difficulties the Board has continued to support high quality studies in Basic Science, Clinical Medicine, and Denistry. Additionally, in a radical and comprehensive review of its funding strategy, the Board has launched important new programmes designed to create enhanced Irish expertise in epidemiologic and health services research. These initiatives stem directly from the wide ranging Corporate Plan for Health Research submitted to the Department of Health, a document which represents a dynamic blue-print for systematically tackling the key health problems and health services issues in Ireland. **The Board is firmly of the view that enlightened State investment in this programme would pay enormous dividends both in the short and long-term.**

Health Research has sometimes been seen as a Cinderella and at times has been overshadowed in the funding prioritisation process by competitors in the area of science, technology, agriculture and veterinary research. The Board is committed to reversing this distorted image by an educational and information campaign which will vigorously make the case that enhanced support for Health Research is a vital national interest.

In examining the relevance of Health Research most commentators would agree that it is essential to have an independent State agency which (1) fosters excellence in the Health Research community, (2) which targets health issues of particular national importance and (3) which critically evaluates the efficiency and effectiveness of health care delivery in Ireland. Never have these areas of responsibility been more crucial than at the present time. Increasing concern has been expressed about the "brain drain" of our best and brightest medical and science graduates, the very constituencies which are so crucial to maintaining a viable research community in Ireland. **It is essential that appropriate research training and job opportunities are available in the Health Research area in order to retain or attract back, our best graduates so that they can contribute to research in this country and so they can ensure an Irish representation in crucially important Research and Development Programmes at an international level within the EEC, the World Health Organisation and other agencies.** In the area of epidemiological research it is clear that many of the diseases that cause premature morbidity and mortality in Ireland and which consume so much of our health care resources are entirely preventable. **Appropriate investment in community health studies, particularly in the area of prevention, would make a major contribution to the health of our people and minimise the burden of such diseases on our health service.** The related area of health services research and health service evaluation is now highly topical and relevant given the urgency of controlling escalating health care costs. **Ireland needs a programme of research into the optimum delivery of efficient and cost effective health care at a primary level, within the community and in our hospital institutions.**

All of these "political" arguments for the greater funding of Health Research in Ireland are necessarily couched in practical utilitarian terms, with a particular emphasis on the likely socio-economic benefit. However, it must not be forgotten that certain other powerful but intangible arguments must be articulated in making the case for the importance of Health Research. Prime amongst these is the concept of fostering excellence, a spirit of scientific enquiry, an urge to limit the boundaries of our ignorance and expand the boundaries of our knowledge and a determination to contribute to an advance in the human condition.

In conclusion, the Health Research Board is optimistic that, with appropriate injection of necessary funding, the exciting and important national research programmes outlined in our Corporate Plan can make a major contribution to fostering excellence in Irish research; to attracting the best and brighest of our graduates to contribute to solving the major health issues of our time; to maintaining a vigorous research community of which the country can be proud; to promoting better community health; and to establishing optimum strategies for the delivery of a humane, personalised efficient and cost effective Health Care Service in Ireland.

August 1990 M.X. FitzGerald

SUMMARY

Dr. V. O'Gorman

Chief Executive,
Health Research Board

The reduction of its grant-in-aid to a level of £1.3 million for 1989 resulted in the Health Research Board being faced with a very lean time in its third year of operation. Following representations by the Board to the Minister for Health, Dr. Rory O'Hanlon T.D., and senior officials of his Department, the budgetary crisis was partially alleviated by having funding responsibility for some of the Board's activities in relation to the Hospital In-Patient Enquiry Scheme, the National Psychiatric In-Patient Reporting System and the Kilkenny Health Project transferred to the Department of Health.

To assist in its forward planning the Board formulated a Corporate Plan for the period 1989-1991 and this plan was submitted to the Minister for Health in March 1989. The Board believes an active research programme to be an essential pre-requisite for the provision of a high quality health service and the plan placed considerable emphasis on the underpinning of health policy with a complementary programme of relevant research. The plan also sought to define a clear and distinctive focus for the Board's future activities and it set out a number of specific corporate goals aimed at enhancing the national R and D capability in medicine and health.

Some 14 highly recommended research projects that had been assessed in Autumn 1988 were initiated but it was not possible to have a call for new research proposals in 1989 due to the severe financial constraints. A compendium of research summaries in respect of research projects completed during 1987 and 1988 was published in November 1989. Through the mechanism of the Summer Student grant scheme 32 medical students were introduced to research techniques and the Science Degree Scholarship scheme enabled two students to complete honours science degrees by availing of an inter-calated year in their medical courses. A total of 31 research projects were successfully concluded in 1989.

With the aid of expert groups, reviews of progress were made in three of the Research Units currently being supported by the Board viz., Affective Disorders, Female Fertility and Excessive Menstrual Bleeding. The results of these reviews confirmed that good progress had been maintained towards achieving the objectives set for these Units and some significant research outcomes are likely to be forthcoming. In the course of the year the work programme of the Drugs in the Elderly Unit was brought to a successful conclusion and the final report of the Unit was launched by Dr. Rory O'Hanlon T.D., Minister for Health, in September. In a foreword to the report the Minister stressed that the research findings should have immediate impact not only in the fields of cardiology and psychiatry but throughout the health services.

In June the Board organised a seminar on Health Services Research (HSR) which was held in Trinity College, Dublin. The seminar provided a forum for policy makers, researchers and the providers of services to have an exchange of views on some of the key issues underlying the development of a health services research programme. Key considerations were identified in terms of definition of needs, measuring activity, assessing outcomes, cost effectiveness, promoting efficiency, the development of performance indicators and the use of incentives in facilitating change.

On the international front six research projects with participation by Irish research groups received funding support from the EC Advanced Informatics in Medicine (AIM) programme. In two of the projects Irish research groups are the prime contractors in the research consortia – Dr. A. McLoughlin, Mid-Western Health Board is developing a Computer Aided Community Oral Health Information System and Dr. J. Malone, St. James's Hospital is working on a Medical Work-station for Intelligent Interactive Organisation and Analysis of Digital Medical Images. The total value of the Irish projects is estimated to be £0.5 million.

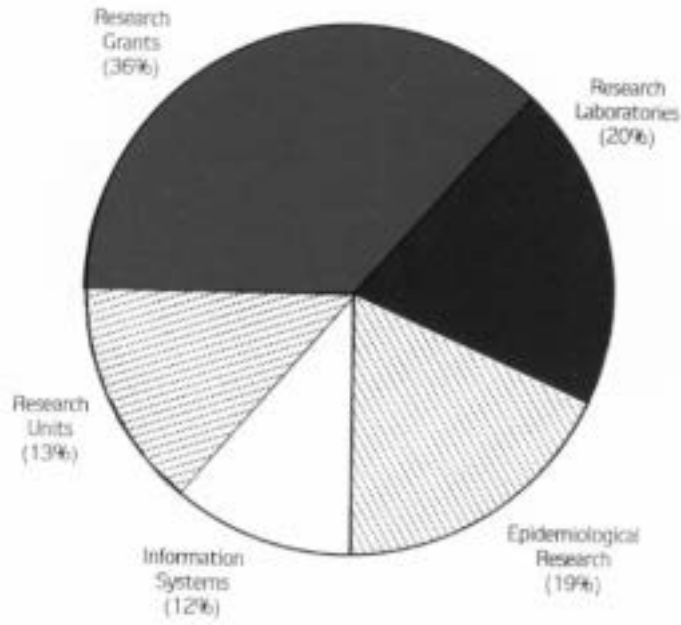
A U.S. funded study on the genetic epidemiology of schizophrenia in the West of Ireland has been extended to the entire country with the aid of additional funding support from the U.S. National Institute of Mental Health. This project is being led by the School of Genetics, Medical College of Virginia, U.S.A. in collaboration with the Board and the recruitment and training of the necessary field, laboratory and administrative staff for the new study was completed by the end of 1989.

The second report of the Travellers Health Status Study "Vital Statistics of Travelling People, 1987" was launched by Mr. Noel Treacy T.D., Minister of State, Department of Health in December. During the year the Board also published two issues of a new newsletter "HRB News" which is intended to provide a wider dissemination of Board sponsored research findings and to increase awareness of the importance of medical and health research issues. Some preliminary work on a fund raising campaign was undertaken and an application for charitable status was submitted to the Revenue Commissioners.

Following confirmation from the Minister for Health that the Board's grant-in-aid for 1990 was to remain at £1.3 million, the Board's Chairman, Dr. W. Watts tendered his resignation to the Minister in November 1989 as he found the funding situation totally unacceptable.

In financial terms, the Health Research Board received a grant-in-aid of £1.3 million from the Government and the allocation between areas of this funding is shown in Figure 1.

Figure 1
Distribution of H.R.B. Research Support



Dr. Vivian O'Gorman, Chief Executive, HRB, Dr. Rory O'Hanlon, T.D., Minister for Health, and Dr. William Watts, former HRB Chairman on the occasion of the presentation of the Board's 1988 Annual Report to the Minister.

RESEARCH GRANTS

Table 1

Research Area	Number of New Projects Funded	Number of Projects Renewed	Total Numbers of Projects Supported
Cancer	-	6	6
Cardiovascular Diseases	3	1	4
Gastroenterology	1	4	5
Haematology	-	2	2
Immunology and Pathology	3	4	7
Microbiology	3	6	9
Mental Health and Neurology	1	4	5
Metabolism and Endocrinology	1	12	13
Pregnancy and Congenital Deformities	-	2	2
Respiratory Diseases	-	2	2
Epidemiology	2	-	2
Total	**14**	**43**	**57**

One of the primary objectives of the Board's research grants scheme is to provide short-term employment and research training opportunities at home for some of our ablest young medical and science graduates. The maintenance of research competence is of considerable importance in the context of having a skilled work-force available to meet the future manpower needs of the Irish health care system.

In 1989, due to the severe financial constraints imposed on the Board, it was not possible to invite any new research grant applications. Having given priority to maintaining funding support for some 43 on-going research projects, the Board decided to fund a small number of highly recommended projects that had been left in abeyance since Autumn 1988.

The distribution of projects by research area and the number of projects funded in each area is outlined in Table 1.

The support of these projects represented a funding commitment of IR£512,912 in 1989. Details of the new projects supported are contained in Appendix F.

Science Degree Scholarships: the scholarship scheme attracted five applications for the 1989/90 academic year. Two scholarships were awarded.

The following candidates accepted the award:
Donogh McKeogh, Physiology, University College, Dublin.
Ivan Casserly, Anatomy, University College, Galway.

Summer Students Grants: a total of 32 awards were made in 1989 at a total cost of £20,480.

1989 Graves Lecture: the twenty-ninth Graves Lecture, sponsored jointly by the Royal Academy of Medicine in Ireland and the Board was given by Dr. Conleth Feighery, Department of Immunology, Trinity College Medical School. The lecture took place in the Academy on the 16th May, 1989 and Dr. Feighery's subject was "Antibody Molecules – Diagnostic Tools and Mediators of Disease".

International Activities

National Institute of Health International Research Fellowships: Four nominations were submitted by the Board for the John E. Fogarty International Research Fellowships for 1989/90 and three awards were made as follows:

These prestigious awards are valued at $20,000 - $30,000 per annum and they are tenable for a period

Name	Visiting	Project
Dr. Christopher McCormack, Zoology, U.C.D.	University of California, Berkeley, California.	Diurnal variations in Dopamine concentration in Teleost Retina
Mr. Henry Redmond, St. Luke's Hospital, Kilkenny.	Mayo Clinic, Rochester, Minnesota.	Motor activity and patterns of accommodation of the rectal ampulla.
Dr. Robert Clarke, Adelaide Hospital	Vanderbilt University Nashville, Tennessee.	Regulatory aspects of platelet metabolism in thrombosis; aspects of unstable angina and occlusive coronary disease.

of two years. The Health Research Board is the designated nominating body in Ireland for these awards.

European Science Foundation (ESF)
The ESF is an international non-governmental organisation, founded in November 1974, with its headquarters in Strasbourg; it currently has 53 member research councils from 19 countries including EOLAS, The Royal Irish Academy and the Board.

The aim of the Foundation is to act as a centre of communication between its member organisations and between individual scientists in Europe; it also seeks to identify areas in which international co-operation could bring most benefit to research in Europe and to provide initial stimulus to collaborative research programmes.

The annual meeting of the Assembly of the European Science Foundation was held in Strasbourg on 21-22 November, 1989. The Board was not represented at the 1989 Assembly.

European Medical Research Councils (EMRC)
The Board is also a member of the Group of European Medical Research Councils, which is a standing Committee of ESF. The 29th annual meeting of the EMRC was held in Madrid, Spain on 8-9 June, 1989. The Board was represented by Professor J. Scott.

European Community (EC)
The 'Management and Coordination Advisory Committee (CGC) in the Field of Medical and Health Research' is the Committee which advises the Council of Ministers of the European Community in this field. The CGC consists of members representing the medical research councils (or equivalents) and the public health bodies of each of the member states; the Irish representation is provided by the Department of Health and the Board.

The Committee supports international collaboration through its concerted action programme on medical and health research which provides funds for working visits, meetings and centralised facilities such as computing and the exchange of reference materials between scientists, within the Community, whose work is already funded by national sources.

In 1989 the Commission completed its assessment of the 600 or so declarations of intent to participate in the 4th EC Medical and Health Research Programme. On the basis of recommendations from its Concerted Action Committees (COMAC's) and Working Parties, the CGC for Medical and Health Research approved the initiation and funding of 54 new concerted action projects in the fields of Cancer (12), AIDS (8), Epidemiology (6), Biology (10), Biomedical Engineering (10) and Health Service Research (8).

Irish researchers will be participating in approximately half of the new projects and Ireland will be the lead country in one of the projects. Dr. Ian Graham, Adelaide Hospital is the project leader for a study relating to the "Epidemiological Assessment of Homocysteinaemia as a Risk Factor for Vascular Disease".

Under the EC Advanced Informatics in Medicine (AIM) programme 43 projects were approved for funding in 1989 and six of these projects involve Irish research groups. All of the projects selected for funding involve consortia of partners drawn from universities, hospitals, research institutes and a wide spectrum of industry from the various Member States. In two of the selected projects with Irish participation, Irish groups are the prime contractors in the consortia. Further details of these projects may be found in the Board's Newsletter – HRB News, No. 2, July 1989.

The Board fulfilled a national representational role in respect of the various EC Committees and Working Parties pertaining to Medicine and Health. The names of Irish national experts serving on the concerted action committees and working parties of the CGC and on other research committees may be found in Appendix C.

RESEARCH UNITS

Professor Brian Leonard

Affective Disorders Research Unit

Director: Professor B. E. Leonard, PhD., DSc., MRIA in collaboration with Professor T. J. Fahy, MD., FRCP., FRCPsych., Professor M. Webb, FRCPI., FRCPsych., Professor K. F. Tipton, MA., PhD., D.C. Williams, PhD., J. O'Donnell, PhD., D. O'Rourke, MB., MRCPsych., S. Barry, MB., MRCPsych., O. H. Phillips, PhD., N. Nic a Bhaird, BA (Mod.), J. P. O'Sullivan, BA. (Mod.), J. Butler, PhD., M. Greally, Bsc., HDipEd., MIBiol., B. O'Neill, BSc. (H).

In addition to the above, contributions to the activities of the Unit have been made by Dr. S. Martens, Professor K. O'Sullivan, Dr. L. Fitzpatrick, Dr. Z. O'Leary, Dr. J. Cooney, Dr. C. Halpin, Dr. I. Daly, Dr. C. Flanagan, Dr. N. All, Dr. D. Healy, Dr. R. O'Toole, Dr. J. McCrodden, Mr. H. Anderson, Ms. M. Tannion, Ms. G. Kagashe and Dr. T. Dinan.

St. Patrick's Hospital and St. James's Hospital, Dublin; Department of Biochemistry, Trinity College, Dublin; Regional Hospital, Galway; Departments of Psychiatry and Pharmacology, University College, Galway.

Establishment Date: 1st January 1986.

Objectives

The aims of this programme are to bring the expertise of a multidisciplinary group, comprising pharmacologists, psychiatrists and biochemists from Galway and Dublin, together in order to investigate the following aspects of depression and its therapy:

(a) The nature of the cause(s) of depression
(b) The mechanisms of action of antidepressant drugs
(c) The development of improved antidepressants
(d) The diagnosis of resistant depression and the nature of the imbalances that give rise to it.

Progress To Date (Summary)

A number of advances have been made since the last report of the Unit in an attempt to fulfil the major components of the research programme which was drawn up nearly five years ago.

1. Brain Research

A brain bank has been established in the Department of Pharmacology, U.C.G. with the aim of collecting post-mortem brains from patients who suffered from different types of psychiatric and neurological disease. So far a number of brains from Alzheimer's patients have been collected from the Dublin region, and an assortment of suicide brains and brains from elderly schizophrenics from the Ballinasloe and Galway areas. A major problem has arisen in attempting to obtain "control" brains (e.g. from cardiac infarct patients). However, an initial study by **J. Butler** has been made covering the density of muscarinic receptors in the right and left portions of several brain regions of the brains so far collected.

This work will continue, comparisons being made of the 5HT2 and beta adrenoceptors on the various neurological and psychiatric groups.

2. Platelet Aggregation

Methodological developments have also occurred in the last year. As the ability of neurotransmitters to cause platelet aggregation is an important technique for investigating changes in receptor function in patients, it is essential that the experimental procedure be standardized. **K. O'Flynn** reports on the sources of variation in platelet aggregation and how these may be standardized.

3. Immune Markers of Affective Disorders

An investigation of aspects of the immune system in psychiatric patients has continued. In the past year, emphasis has been placed on changes in monocyte phagocytosis as these cells are an important source of both the prostaglandins and lympokines, substances which play a key role in orchestrating the behaviour of other types of lymphoid cells in this immune response. Unlike the polymorph neutrophils whose activity is decreased in depressed, manic and schizophrenic patients and is largely normalized following effective treatment, the monocyte phagocytic activity is increased before treatment and is only normalized in the depressed patients who respond to treatment.These findings suggest that depressed polymorph phagocytosis may be a state marker of treatment response in these major psychiatric disorders, whereas enhanced monocyte phagocytosis is a state marker of depression but a trait marker of schizophrenia and mania. It is not without interest that qualitatively similar changes are found in the olfactory bulbectomized rat model of depression to those seen in depressed patients. These findings are reported by **McAdams and Leonard.**

4. Changes in Neuroendocrine Function
The effect of chronic treatment with antidepressants on the behaviour and neuroendocrine status of intact and bulbectomized rats has been the subject of detailed studies. In brief, chronic cannulation of rats (both intact and olfactory bulbectomized), has enabled changes in the neuroendocrine status of the animals to be investigated at different times during the chronic administration of 'standard' and 'novel' anti-depressants.

Growth hormone, corticosterone and prolactin levels can now be quantitatively determined following a clonidine, desipramine and serotonin agonist challenge. Distinct differences would appear to occur following chronic desipramine and sertraline treatments thereby enabling the effects of antidepressants on specific receptors controlling the endocrine status to be evaluated. This study forms the basis of a report by **Greally and O'Donnell.**

The effects of various novel antidepressants on the behaviour and biochemistry of the olfactory bulbectomized rat have continued. The introduction of a method enabling serial blood samples to be removed from the retro-orbital sinus of rats has enabled the changes in serotonin transport into platelets to be determined following acute and chronic treatment. The result of these studies show that antidepressants increasing or decreasing the uptake of serotonin after acute treatment have qualitatively similar effects after chronic treatment in that they enhance the serotonin uptake. The effect of bulbectomy on monocyte phagocytosis has also been investigated; as in depressed patients, bulbectomy results in an enhanced phagocytic response in these animals. These findings are reported by **Kelly and Leonard.**

5. Panic Disorder Study
The main clinical studies undertaken by the Galway Section of the Unit have consisted of detailed profiling of the clinical and biochemical response of 66 panic patients over a three month period to placebo, lofepramine or clomipramine. This three year study is now complete and detailed statistical analysis of the results are currenly underway. In brief, it would appear that both antidepressants are equally effective in attenuating the main symptoms of panic; some of the changes in neurotransmitter function on blood cells appear to resemble qualitatively these found in patients with endogenous depression. It is clear that changes in serotonin receptor function, and transport, are abnormal in panic and only partially corrected by effective drug treatment. A summary of these findings is given by **O'Rourke and Fahy** (clinical study) and **Butler and Leonard** (biochemical study).

6. Neuroendocrine Studies in Depressed Patients
The clinical section of the Dublin Unit, under the direction of Ted Dinan, has continued to make major advances in probing the changes in neuroendocrine regulation in various types of psychiatric and neurological diseases. This has resulted in some 14 publications over the last year and an outline of the major areas covered are contained in the report by **Dinan.** One of the major developments has been in the examination of the endocrine status in post-stroke depression; a blunting of the proactin response to buspirone challenge suggests that 5HT1A receptors may be abnormal in this condition. It was also shown that patients with post-stroke depression are highly resistant to antidepressant treatment. In a collaborative study with Clive Williams (TCD), it was found that patients with post-stroke depression do not show an abnormality in 3H-5HT transport into platelets. Clearly this is an important sub-group of depressed patients that may differ in the malfunctioning of their serotonergic system from patients with endogenous depression. The St. James's group have also extended their studies of various 'probes' to investigate the effect of serotonin and cholinergic receptor agonists on neuroendocrine responses in patients with affective disorders. Undoubtedly these findings are of fundamental importance to our understanding of the changes in the neurotransmitter status of such patients and may ultimately be of diagnostic value.

7. Monoamine Oxidase Inhibitors
Studies on the mechanism of action of monoamine oxidase (MAO) inhibitors and an investigation of the various ways in which the side effect profile of these drugs may be improved has been the subject of series of studies by **K. Tipton and his group.** An important development this year has been the improvement in the method for quantifying MAO-A and MAO-B forms of the enzyme in relatively small tissue samples. The establishment of such assays should allow an investigator to study the relationship between changes in sub-types of MAO in affective disorders. The productivity of this Section of the Unit is shown by the 10 publications that have resulted from their endeavours over the last year.

8. Characteristics of Serotonin Transport Site
Clive Williams and Orla Phillips have continued to make progress in characterizing the nature of the serotonin carrier on the human platelet membrane in animal brain. Anti-idiotypic antibodies have been prepared in an attempt to recognize tricyclic antidepressant binding sites that are associated with

the serotonin uptake on platelet and synaptosomal membranes. An additional aim of this approach is to develop an immuno assay for tricyclic antidepressants. While considerable progress has been made in the identification of this impramine binding site using such methods, it would appear that the antisera also reacts with muscarinic receptor sites. It is also possible that the serotonin binding site is not identical with the serotonin transport site and therefore uncertain whether serotonin and impramine bind at the same sites on the serotonin carrier.

In conclusion, despite the severe restriction in funding to the Unit, there have been satisfactory developments both in the laboratory and in the clinical studies. Since the last report some 33 full manuscripts have either been published or are in the process of publication.

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Professor Kevin O'Malley

Drugs in the Elderly Research Unit

Director: Professor Kevin O'Malley, MD., PhD., FRCPI., FRCPE., in collaboration with Dr. J. Waddington, MA., MSc., PhD.; Dr. J. Docherty, BSc., PhD.; Dr. E. O Brien, MD., FRCP., FRCPI.; Dr. J. Kelly, BSc., PhD.; Dr. T. Cotter, BSc., PhD.; Dr. C. O'Boyle, BSc., PhD.; Dr. K. O'Boyle, BSc., PhD.; Dr. D. Coakley, MD., FRCPI.; Dr. B. Walsh, MRCPI.; Dr. J. Cox, MRCPI.; Dr. P. McCormack, MRCPI.; Ms. L. Hyland, BSc.; Dr. S. Kilfeather, BSc., PhD., Ms. L. Nolan, BSc. (Pharm); Dr. H. A. Youssef, DPM., MRCPsych.; Dr. P. McKeon, MD., MRCPsych.; Dr. S. J. Cooper, MD., MRCPsych.

Royal College of Surgeons in Ireland, Beaumont Hospital, Dublin, St. James's Hospital, Dublin, St. Davnet's Hospital, Monaghan, St. Patrick's Hospital, Dublin, Department of Mental Health, Queen's University of Belfast.

Completion Date: The work of this Unit concluded on 31st March, 1989.

Objectives

The Unit carried out a comprehensive investigation into drugs in the elderly under the following five headings:

1) prescribing
2) compliance
3) adverse reaction
4) therapeutic effect/pharmacodynamics
5) pharmacokinetics/drug handling

It examined in some detail the special problems that pertain to two therapeutic areas – high blood pressure and psychiatric disease.

Main Findings

Some of the key findings of this research programme include:

(i) Overall cardiovascular control is little changed by ageing in the absence of disease processes, but there is diminished adaptability.

(ii) The doses and duration of treatment with tranquillisers such as benzodiazepines in the elderly is excessive.

(iii) Overuse of digoxin in the treatment of heart failure is apparent and it was estimated that digoxin could be withdrawn from 34-44% of patients studied. Many patients with atrial fibrillation, where digoxin is very effective, had sub-therapeutic doses of the drug.

(iv) The risk of adverse drug reactions can be minimised by avoidance of unnecessary polypharmacy.

(v) Vulnerability to tardive dyskinesis (abnormal involuntary movements) increases with age in association with signs of organic brain dysfunction

and appears on the basis of preclinical studies unrelated to the mechanism of the antipsychotic efficacy of neuroleptics.

Additional Benefits
A total of 120 scientific publications resulted from the work of the Unit. Senior members of the group contributed many invited chapters and sections in books and journals and furthermore the grant facilitated the group getting involved in other areas of research that hold promise for the future.

Finally ten academic members of staff obtained higher degrees (MDs and PhDs) relating to work carried out on the grant. Also the training obtained by these young researchers hopefully will be put to good use in research in the universities and health care system in the years to come.

The final report of the Unit was published by the Board in September 1989 (Research Unit Report No. 1) and in a foreword to the report Dr. Rory O'Hanlon T.D., Minister for Health, stated "it is to be hoped that this report will be made available to all doctors and other appropriate health professionals, not only in the fields of cardiology and psychiatry where the findings should have an immediate impact, but throughout the health services".

Professor Patrick Fottrell

Female Fertility Research Unit

Director: Professor P. F. Fottrell, PhD., DSc., in collaboration with Professor E. M. O'Dwyer, MAO, FRCOG., FRCPI.; Prof. F. Meehan, FRCOG.; Dr. J. P. Gosling, PhD.; Dr. I. Bolaji, MBBS., MRCOG., and Mr. D. F. Tallon, MIBiol.

Department of Biochemistry, University College, Galway.

Establishment Date: 1st January, 1986.

Objectives
The overall objectives of this Unit are:

(i) development and validation of rapid, non-isotopic, solid phase immunoassays for reproductive hormones in serum and saliva

(ii) investigate the clinical applications of such assays in areas such as female infertility.

Progress To Date (Summary)
During 1989 a solid phase enzymeimmunoassay for salivary testosterone was developed and fully validated in the laboratory. Considerable emphasis was placed during the year on investigating the clinical applications of salivary progesterone and oestrone enzymoimmunoassays in the following areas:

(a) assessment of the return of post-partum fertility

(b) diagnosis and assessment of therapy for spontaneous recurrent abortion

(c) pharmacokinetic studies on the bioavailability of Premarin and micronised oral progesterone which are used in hormone replacement therapy.

Return of Post-Partum Fertility
Progesterone and oestrone were measured in daily samples of saliva taken from 20 lactating and 10 non-lactating women until the resumption of at least two menstrual periods. The pattern of breastfeeding was recorded daily and serum prolactin and progesterone were measured at two or three weekly intervals. Some lactating mothers also kept charts on basal body temperature and cervical mucus changes.

Ovulation was inferred when salivary progesterone rises above 251 pmol/L and remained sustained for at least three days. The day of ovulation was determined by cumulative sum analysis and the luteal phase was assessed by interfacing the target salivary profiles within 5th and 95th percentile of a control corridor. Data from this study are being analysed.

Diagnosis and Assessment of Therapy for Spontaneous Recurrent Abortion
This is a joint study with the Department of Obstetrics and Gynaecology, Erinville Hospital, University College Cork and the Royal Shrewsbury Hospital, Shrewsbury, U.K. The initial objective was to establish a normal range of salivary progesterone concentrations in the first trimester of pregnancy. Eight patients have completed sampling and the data are being analysed. Progesterone was measured in daily saliva samples over 13 consecutive menstrual cycles in fifteen women under investigation for spontaneous recurrent abortion. Luteal phase defects were detected in three patients. Pregnancies resulted in three others but two terminated spontaneously while another is ongoing. The three pregnancies were supported by progesterone

therapy. Data from these studies are being analysed.

Pharmacokinetics

Salivary oestreone and progesterone were measured in 40 postmenopausal women undergoing hormone replacement therapy with Premarin and micronised oral progesterone. Ten women who took 100 mg of micronised progesterone daily per orally had a baseline salivary progesterone concentration of 284.3 (32) pmol/L before treatment and 1857.7 (149) pmol/L at a mean peak time of 113.3 min. after treatment. Data from these studies are being analysed but preliminary results indicate that salivary progestrone analysis provides a cost effective non-invasive procedure for doing pharmacokinetic studies of this type.

Publications

Finn, M.M., Gosling, J.P., Tallon, D.F., Joyce, L.A. Meehan, F.P. and Fottrell, P.F. Follicular growth and corpus luteum function in women with unexplained infertility, monitored by ultrasonography and measurement of daily salivary progesterone. Gynecol. Endocrinol., 3, 297-308, 1989.

Howard, K., Kane, M., Madden, A., Gosling, J.P. and Fottrell, P.F. Direct Solid-Phase Enzymeimmunoassay of Testosterone in Saliva. Clinical Chemistry, 35, 2044, 1989.

Professor Brian Sheppard

Professor John Bonnar

Excessive Menstrual Bleeding Research Unit

Directors: Professor Brian L. Sheppard, MA., MSc., DPhil., MRCPath. and Professor John Bonnar, MA., MD., FRCOG., in collaboration with Dr. S.C. Sharma, MA., MSc., PhD., Sr. M.E. Carroll, Dr. L. Daly, PhD. and Dr. M. Stack, PhD. with contributions from Nurse B. Hennelly and Ms. M. Jordan.

TCD Department of Obstetrics and Gynaecology, and Department of Pharmacology and Therapeutics, Sir Patrick Dun Research Centre, St. James's Hospital.

Establishment Date: 1st July, 1987.

Objectives

The unit is studying local uterine factors that contribute to normal and excessive menstrual bleeding – structural and functional aspects of haemostasis including endometrical blood vessels, coagulations, fibrinolysis and platelets as well as histamines, prostaglandins and steroid receptors – in order to obtain a better understanding of the regulation of uterine bleeding. The long term objectives are to gain a better therapeutic control over this process, reducing the need for treatment by hysterectomy.

Progress to Date (Summary)

Three hundred and fifty women, aged 30-50 years, have now been recruited into the study from patients complaining of excessive menstrual bleeding attending Gynaecology Out-Patient's Clinics. Menstrual blood loss in a minimum of two consecutive cycles have been measured in 260 of these patients of whom 148 (57%) were found to have a normal menstrual loss of less than 80 ml (x 36.9 ml, range 3-76.5) and 112 (43%) were found to have excessive menstrual blood loss of greater than 80 ml per cycle (x 197.5 ml, range 82-1,059). Of these patients 95 have undergone hysterectomy; 40 (42%) had normal menstrual blood loss and 55 (58%) had excessive menstrual bleeding. Histological examination of the uteri from the latter group showed that 68% had no pathology and were classified as dysfunctional uterine bleeding (DUB) and 32% had evidence of uterine pathology.

Analysis of peripheral blood has shown that in patients with DUB enhanced fibrinolysis occurs in the late secretory and menstrual phases of the cycle and an association exists between both the activator and inhibitor of fibrinolysis and the degree of uterine bleeding. As yet, however, no coagulation or fibrinolytic factors in menstrual blood have shown any positive correlation with the amount of menstrual blood loss during the first two days of menstruation.

Biopsies of the uterus taken at hysterectomy showed levels of the activator of fibrinolysis, measured as tissue plasminogen activator antigen (t-PAag) were higher in the myometrium than in the endometrium throughout the menstrual cycle. The highest levels of t-PAag were found in the endometrium and myometrium of patients with DUB in the late secretory phase: in the endometrium these levels were significantly higher than in women with normal menstruation. The levels of t-PAag in late secretory endometrium showed a significant, positive correlation with the degree of menstrual blood loss suggesting that increased fibrinolytic activity in uterine endometrium, prior to

the onset of menstrual bleeding, plays an important role in the pathogenesis of DUB. The site of production of the fibrinolytic activator (t-PA) has been localised to endothelial cells of endometrial and myometrial vasculature.

Monoclonal antibodies together with the peroxidase anti-peroxidase technique were used to localise the steroid receptors of oestrogen and progesterone in the uterine wall. Assessment of the staining intensity in the various cell types and the numbers of cells positively staining are currently being undertaken to ascertain a possible relationship between dysfunctional uterine bleeding and changes in oestrogen and progesterone receptor content throughout the normal menstrual cycle.

Histological examination by light microscopy has shown no variation in vascular density in the uterine wall through the menstrual cycle. However, a more detailed examination of endometrial vasculature expressed as volume density is at present being undertaken in these patients.

Ultrastructural studies have been limited to detailed examination of endometrial vasculature, and peri-vasculature changes, during the pre-menstrual and menstrual phases of the cycle in normal menstruation and in DUB. Electron microscopy has shown defective haemostasis in normal menstruation, with an absence of haemostatic plugs in the pre-menstrual phase and small platelet plugs in early menstruation.

During the past year good progress has been made in fulfilling the original aims of the Unit. Analysis of the data so far has shown certain trends and in some parameters significant differences in local uterine haemostatic factors between subjects with normal menstruation and those with DUB. Particularly striking, have been differences in tissue plasminogen activator antigen levels in the endometrium of the late secretory phase of the cycle, together with differences in peripheral blood levels of tissue plasminogen activator antigen and plasminogen activator inhibitor in the two groups of subjects. These factors correlate with the degree of menstrual blood loss, and possibly along with endothelial vascular defects, may play a crucial role in the mechanism of increased menstrual bleeding.

Publications

Daly, L., Sheppard, B.L., Carroll, E., Hennelly, B. and Bonnar, J. Coagulation and fibrinolysis in peripheral blood throughout the menstrual cycle in women with normal and dysfunctional uterine bleeding. Irish J. Med. Sci. In press.

Sheppard, B.L. Stack, M., Jordan, M. and Bonnar, J. Plasminogen activator in the human uterus through the normal menstrual cycle and in dysfunctional uterine bleeding. Irish J. Med. Scri. In press.

Jordan, M., Sheppard, B.L. and Bonnar, J. Immunocytochemistry of oestrogen and progesterone receptors in the uterus of women with normal and excessive menstrual bleeding. Irish J. Med. Sci. In press.

Sharma, S.C., Sheppard, B.L. and Bonnar, J. Endometrial tissue levels of PGE_2 and PFG_2 metabolites in women with normal menstruation and dysfunctional uterine bleeding. Irish J. Med. Sci. In press.

Dr. Barry Bresnihan

Rheumatoid Arthritis Research Unit

Directors: Dr. B. Bresnihan, MD., FRCP., FRCPI.; Dr. C. Feighery, MD., FRCPI. and Dr. A. Whelan, Ph.D.

Department of Rheumatology, St. Vincent's Hospital, Dublin.
Department of Immunology, St. James's Hospital, Dublin.

Establishment Date: 1st January, 1986.

Objectives

The objectives of this programme are:

1) to further study the role of rheumatoid factor in rheumatoid arthritis and its possible immunoregulatory function as mediated by its interaction with Fc receptors on lymphocyte surface membranes
2) to determine if associations exist between immune aberrations including those induced by rheumatoid factors and the immunohistological features, disease progression and response to treatment of a series of well characterised patients with rheumatoid arthritis.

Progress to Date (Summary)

Aspects of cell migration to synovial membrane were

examined by analysing the mononuclear cell composition of focal perivascular lymphoid aggregates of different sizes. Synovium was obtained at arthroplasty from 19 patients with rheumatoid arthritis and examined for vascular endothelium and several mononuclear cell populations. The results of this study demonstrates that the cellular composition of focal perivascular lymphoid aggregates in group A was dependent on aggregate size and different substantially from the diffuse cellular infiltrates present in group B. Thus, B cells and plasma cells accumulated only in larger focal aggregates. Monocytes and activated T cells characterised diffuse interstitial infiltration of the synovium irrespective of whether focal perivascular aggregates were present.

In vitro cytokine and rheumatoid factor (RF) synthesis by synovium demonstrating different immunohistologic patterns was examined. Synovium was obtained from 22 patients at arthroplasty. Fifteen demonstrated focal perivascular lymphoid aggregation (group A); 7 demonstrated diffuse mononuclear cell infiltration (group B). Measurements of standard clinical and radiologic parameters were similar in both groups. This study demonstrates an association between the presence of perivascular lymphoid aggregation and increased synovial in vitro synthesis of cytokines. The formation of perivascular lymphoid aggregates seen in some synovial tissue samples may represent an immunologic mechanism which differs from that resulting in diffuse mononuclear cell infiltration.

IL-1β is predominantly a product of macrophages and monocytes. In previous studies synovial levels of IL-1β correlated with clinical measures of synovitis in individual joints. Further study was undertaken in order to compare synovial IL-1β levels with histologic features of synovitis. Synovial fluid (SF) was obtained from the knee joints of 11 patients with active untreated RA. Needle biopsies of the synovial membrane (SM) were obtained at the same time. IL-1β was measured by radio-immunoassay. A specific correlation between SF IL-1β levels and synovial lining layer thickening was demonstrated and this is consistent with the previous observation of intense accumulation of macrophages in the lining layer. It is suggested that the synovial production of IL-1β results predominantly from the migration of macrophages into the synovial lining layer. The correlation between SF IL-1β and IgG may reflect a stimulatory effect on SM B cells.

Immunohistologic features which might predict the clinical course and outcome of rheumatoid arthritis were sought by examining multiple synovial membrane samples obtained by needle biopsy from the knee joints of 57 patients who had not received disease-modifying antirheumatic drugs. Clinical measurements, but not biopsies, were repeated 1 year and 3 years after commencing treatment. A correlation between both the intensity and synovial lining layer thickening ($p < 0.01$) and mononuclear cell infiltration ($p=0.02$) and the clinical status at the time of biopsy was observed. After 3 years of treatment the correlations were maintained in patients who had presented and persisted with milder disease ($p < 0.01$), but not in patients who had presented with more active disease.

A number of studies were undertaken in order to examine endothelial cell function in rheumatoid synovial membrane. Synovial tissue from both inflamed and non-inflamed knee joints of 13 patients with untreated RA were examined for vascular proliferation and morphologic alteration of endothelial cells. Perivascular mononuclear cell infiltration and increased synovial lining layer thickness were observed in tissue from both inflamed and non-inflamed RA joints. However, vascular proliferation and morphologic alteration of endothelial cells to resemble high endothelial venules (HEV) were observed only in tissue from inflamed RA joints. These observations suggest that migration of mononuclear cells from the peripheral blood to the perivascular areas and lining layer occurs prior to vascular proliferation and morphologic alteration of endothelial cells.

Angiotensin converting enzyme (ACE) may be a marker of endothelial cell function. In a previous study angiotensin converting enzyme was increased in the synovial fluid of patients with inflammatory joint disease when compared to controls. This suggested local ACE production by the RA vasculature. In a further study, synovial membrane and synovial fluid were obtained at arthroplasty from 12 patients with sero-positive RA. Undigested SM was cultured for 7 days and ACE activity levels were measured in the culture supernatants at day 1, day 7 and in the SF. While this study suggests that ACE is produced by the rheumatoid SM, the synthesis may reflect increased EC activity rather than membrane vascularity.

A variety of studies aimed at examining the function and production of rheumatoid factor were completed. Induction of IgM-rheumatoid factor (IgM-RF) as a result of certain infections has been extensively reported. The Group sought to examine the specificity of the circulating IgM-RF induced in several infectious

conditions and autoimmune states. The findings suggest that in chronic autoimmune conditions, RF with Fc specificity is predominant in the circulation. In contrast, induction of Fab directed RF is predominant in patients with Infectious Mononucleosis and Cystic Fibrosis (CF).

IgA rheumatoid factor may be an important component of tissue defence at the site of mucosal barriers. In a large cohort of patients with cystic fibrosis we previously reported the presence of circulating IgA rheumatoid factor in 37%. In a further study the specificity of IgA-RF was examined in 13 CF patients with acute bacterial infection. This study demonstrated that the specificity of IgA-RF produced following acute bacterial infection in CF differs from other inflammatory and infectious diseases.

A subset of B cells demonstrating the CD5+ surface marker has been reported as the major producer of autoantibodies including rheumatoid factor. CD5+ B cells and TCR γδ+ T cells have been reported to be coordinately elevated in patients with RA. A study was undertaken to assess the circulating levels of these cell types in two groups of patients at the onset of rheumatoid arthritis: group 1 presenting before the age of 45 years and group 2 after the age of 65 years. All patients had active disease and were not receiving disease remittive agents at the time of study. This study demonstrated the coordinate expansion of the CD5+ B cells and γδ+ T cell types in the peripheral blood of patients with RA presenting before 45 years of age and not after 65 years of age.

Gold therapy is known to cause a significant reduction in the level of rheumatoid factors in patients with rheumatoid arthritis. The CD5+ B cell levels and TCR γδ+ T cell levels in RA patients not receiving remittive therapy and patients treated with gold sodium thiomalate (GST) were examined. The findings suggest that gold therapy may reduce the levels of RFs by selectively affecting CD5+ B cells.

Further insight into the relevance of CD5+ B cells in rheumatoid factor production was obtained from a study of patients with infectious mononucleosis (IM). IM is a self-limiting disease caused by the Epstein Barr virus (EBV) and is often characterized by the presence of circulating autoantibodies such as rheumatoid factor, antinuclear antibodies and the presence of heterophile antibodies. Autoantibodies are thought to be the product of CD5+ B cells which have been found to be raised in autoimmune conditions such as rheumatoid arthritis (RA) and Sjogren's syndrome. Since EBV has been implicated in the pathogenesis of RA, patients with IM were examined for the presence of CD5+ B cells and RFs. These studies suggest that the increased numbers of CD5+ B cells and the concommnitant production of autoantibodies may simply reflect a perturbance of the immune response in patients with IM.

Publications

Rooney, M., Whelan, A., Feighery, C. and Bresnihan, B. The immunohistologic features of synovitis, disease activity and in vitro IgM rheumatoid factor synthesis by blood mononuclear cells in rheumatoid arthritis. J. Rheumatol., 16, 459-467, 1989.

Rooney, M., Whelan, A., Feighery, C. and Bresnihan, B. Changes in synovial membrane mononuclear cell infiltration correlate with rheumatoid factor production by blood mononuclear cells and with the clinical course of rheumatoid arthritis. Arthritis Rheum., 32, 361-369, 1989.

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Hassan, J., Feighery, C., Bresnihan, B. and Whelan, A. Expression and regulation of the HLA-DR antigen on circulating monocytes isolated from patients with rheumatoid arthritis. Arthritis Rheum., 48, 443-445, 1989.

Soden, M., Hassan, J., Scott, D.L., Hanly, J.G., Moriarty, M., Whelan, A., Feighery, C. and Bresnihan, B. Lymphoid irradiation in intractable rheumatoid arthritis: long-term follow-up patients treated with 2000 rad and 750 rad. Arthritis Rheum., 32, 523, 1989.

Coffey, M., Hassan, J., Feighery, C., Fitzgerald, M. and Bresnihan, B. Rheumatid factors in cystic fibrosis: associations with disease manifestations and recurrent bacterial infections. Clin. Exp. Immunol., 77, 52-57, 1989.

Bresnihan, B. Immunohistologic studies of the synovial membrane in rheumatoid arthritis. J. Irish Coll. Phys. Surg., 19, 124-127, 1990.

Hassan, J., Feighery, C. Bresnihan, B., Whelan, A. increased CD5+ B cells in patients with infectious mononucleosis. Brit. J. Haematology, 74, 375-376, 1990.

Soden, M., Whelan, A., Feighery, C. and Bresnihan, B. Lymphocyte infiltration and the synthesis of IgM and IgA rheumatoid factors by rheumatoid synovial membrane. Rheumatol. Int., 1990 (in press).

Fitzgerald, O., Soden, M., Yanni, G., Robinson, R., Bresnihan, B. Morphometric analysis of blood vessels in synovial membrane obtained from the clinically involved and uninvolved knee joints of patients with rheumatoid arthritis. Ann. Rheum. Dis., 1990 (in press).

Pictured on the occasion of the 1989 Graves Lecture at the Royal Academy of Medicine in Ireland are Professor Patrick Collins, Dr. John Fleetwood, Professor John Dundee, President of the Academy, Dr. Conleth Feighery, 1989 Graves Lecturer and Dr. William Watts, Health Research Board.

HEALTH INFORMATION SYSTEMS

The Board currently administers two health information systems namely the National Psychiatric In-Patient Reporting System and the Three County Psychiatric Case Register. Responsibility for the administration of a third system, the Hospital In-Patient Enquiry Scheme (H.I.P.E.), was transferred from the Board to the Department of Health from 1st January 1989.

The National Psychiatric In-Patient Reporting System (N.P.I.R.S.) is an on-going in-patient reporting system established by the Board in 1971 and it has full national coverage which involves the collection and processing of approximately 29,000 cases per annum. An annual report entitled "Activities of Irish Psychiatric Hospitals and Units" is published.

In 1989 N.P.I.R.S. continued to report on admissions to, and discharges from, Irish psychiatric hospitals and units. The reports for the years 1986 and 1987 were published during 1989.

The N.P.I.R.S. System was funded directly by the Department of Health in 1989.

The Three County Psychiatric Case Register is the complement to the hospital reporting system, in that it provides longitudinal information on the use of all psychiatric services in defined geographical areas. The three counties (Carlow/South Kildare, Roscommon and Westmeath) reflect rural service-provision in three areas of Ireland and a fourth register, in the St. Loman's catchment area of the Eastern Health Board, provides information on service-provision in an urban area.

The information recorded in the register is cumulative, longitudinal and person-linked so that individual groups of patients with common characteristics can be followed over periods of time. The register data provide a valuable input to planning and administration of psychiatric services and have proved invaluable for epidemiological research.

Attending the launch of the Board's 1988 Annual Report were: Mr. Colm O'Sullivan (Board Member), Dr. Timothy O'Dwyer (Board Member), Dr. Joseph Barry (Eastern Health Board) and Mr. Donal Nevin (Board Member).

EPIDEMIOLOGICAL STUDIES

The current range of activities in this area relate to studies undertaken by senior staff employed directly by the Board. Several of the studies provide a national input to programmes being co-ordinated by the European Community. The existing activities may be broadly classified as follows:

(a) Mental Health Studies
(b) Mental Handicap Studies
(c) Perinatal Epidemiology and Child Health
(d) Travellers' Health Status Study
(e) EUROCAT

More specific information on the current status of these studies is outlined below:

(a) Mental Health Studies
Dr. D. Walsh, MB, DPM, FFCM, FFCMI, FRCPsych, FRCPI
Ms. A. O'Connor, M.Soc.Sc.
Health Research Board.

Roscommon Family Study of Schizophrenia
The Roscommon Family Study consists of a survey of two groups of patients, one group with a schizophrenic illness and the other group with an affective illness, compared to matched controls selected from the community. The survey also included all the first-degree relatives of both patients and controls. The work on the study continued throughout 1989 and is expected to be completed in 1990. The study is being carried out jointly between the Health Research Board, the Western Health Board and the School of Genetics, Medical College of Virginia and is based in St. Patrick's Hospital, Castlerea, County Roscommon.

The basic hypothesis being tested is that a greater prevalence of schizophrenia or schizophrenia like disorders will be found in the relatives of schizophrenic patients than in those of affective patients and of normal controls. In addition the study will determine whether family distribution of schizophrenia in Ireland is any different from elsewhere.

High Density Study: The High Density Study is an extension of the Roscommon Family Study. The latter had identified families which were multiply affected by schizophrenia and these families were the subject of additional study within the Roscommon Family Study. An application for funding was then made to the U.S. National Institute of Mental Health for the extension of this high density study to the whole of Ireland. In October 1989 the Board learnt that funding had been approved for a further two year period.

This study is now in progress and the work is co-ordinated from four research stations in Dublin (study headquarters), Limerick, Kilkenny and Belfast. Laboratory facilities are provided at the National Cell and Tissue Culture Centre in Dublin City University. Currently there are 10 staff employed on this study including a Project Coordinator, Psychiatrists, Phlebotomists, Interviewers and Secretarial Staff. Work is expected to continue to the end of 1991.

Ascertainment of Suicide
The work on suicide in Ireland which is examining the question of whether the recent reported increase in suicides are real or apparent has been completed and is shortly to be published in Psychological Medicine.

Health Care of the Elderly
Ireland has participated in an EC study of service-delivery to the elderly through the joint working of the Health Research Board, the North-Western Health Board and the Department of Health.

Two studies were conducted within the North-Western Health Board region. The first was a survey of elderly people living at home and the second was an intensive study of elderly persons referred for non-acute residential care from the same geographical districts. An unpublished report has been made available to the Irish steering committee on each of these two studies and further information has been made available for the international comparison reports being compiled by the EC co-ordinators of the project.

EC Studies on Mental Health Topics
In spite of initial involvement with, and planning of, EUROMAT (Maternal Alcohol Consumption and Pregnancy Outcome) and EURODEM (an epidemiological study of dementia in the elderly, the Board has been forced to drop participation in these projects because of the lack of funding.

The Board has now become involved in a small planning group concerned with Mental Health Evaluation in the Community, which it is hoped will become a concerted action project and in which the Board hopes to continue to participate.

Studies of Drug Misuse
Mrs. A. O'Hare, M.Soc.Sc.
Ms. M. O'Brien, B.A.

EPIDEMIOLOGICAL STUDIES

Dublin Drug Misuse Reporting System
This reporting system, funded by the European Commission (EC) and the Department of Health, commenced operation in August 1989. By the end of that year 19 centres were participating in the system and returning anonymous information to the Health Research Board on clients treated by them. This level of participation involved almost all centres who provide treatment to drug misusers in the Greater Dublin area. The objective of this data collection is to obtain basic epidemiological information on the extent of treated drug misuse in a defined catchment area; to monitor changes over time; to provide feedback to the participating centres and to the Department of Health; to facilitate the development/assessment of treatment policies and to provide an input to the multi-city programme of drug misuse initiated by the Pompidou Group, Council of Europe. An overview of earlier completed work in this epidemiological project in which Dublin was a participating centre has recently been published.[1]

The Dublin/London Drug Research Project
The participation of Dublin in this particular study was dependent on the existence of a reporting system to collect the required information on drug misuse. Funding for the project came from the EC, the Irish Department of Health and the British Department of Health and Social Security.

The broad objective of the study was to test the feasibility of collecting similar core data on treated drug misuse in both cities. The groundwork for this project had been completed in work undertaken by seven European cities between 1982-1986.[2] The more specific aims of the study were to obtain data on the "first treatment demand" indicator which was shown to be a valuable indicator of drug activity and of the demand on treatment services. The fieldwork was carried out in both cities during the month of August 1989 and a report submitted to the EC by the end of October 1989.

Encouraged by the success of this pilot undertaking in Dublin and London the Pompidou Group plan to extend collection of similar information, within an agreed common framework of concepts, definitions and instructions to a further 8-10 European cities.

(b) Mental Handicap Studies
Dr. D. Kavanagh, MRC,Psych.,DCH.
Dr. V. Keane, MRC,Psych.

Community Based Residence for Mentally handicapped People
Analysis of the data collected in the study of Community Based Residences for Mentally Handicapped People (CBR's) was completed during 1988. The final report on this study has been delayed due to changes in personnel and publication is now expected in 1990.

Survey of Adults with Down's Syndrome in a Community Care Area
Down's Syndrome is a common cause of mental handicap with a prevalence of 1.03:1,000 total population in 1979[3].

Many individuals so affected have physical problems including obesity, hearing problems, eye problems, thyroid problems and cardiac problems. Psychiatric problems also affect the people with Down's Syndrome, namely emotional and behaviour problems, affective disorders, schizophrenia and Alzheimer's disease.

The purpose of the present study is to determine the nature and frequency of physical and psychiatric morbidity in an adult population of Down's Syndrome.

The population in this study is made up of all the people with Down's Syndrome who were 16 years and over in December 1986 and living in a Community Care Area of Dublin. This was obtained by direct contact with Community Care personnel together with the various service agencies involved, whose help we gratefully acknowledge.

This study commenced in 1986 but due to personnel changes it was interrupted for some 18 months until January, 1989. To date 22 people have been assessed. Presently consideration is being given to expanding the study into the area of Alzeimer's disease + Down's Syndrome. A preliminary report will be ready for publication in 1990.

(c) Perinatal Epidemiology and Child Health
Dr. P. Kirke, MB,FFCMI, FFCM, MSc, DCH, DObst.
Health Research Board.

Irish Vitamin Study
The Irish Vitamin Study is a randomized clinical

trial to determine whether periconceptional supplementation with either a multivitamin preparation alone or folic acid alone can reduce the risk of recurrence of neural tube defects from 5% to 1% or less in mothers with a previously affected baby. Randomization ended in 1988 and the closing date for entry of pregnancy outcomes for analysis in the trial was 31 December, 1989. The findings of the trial will be prepared for publication in 1990.

Neural Tube Defect Follow-up Project

All mothers who delivered a baby with a neural tube defect (NTD) during 1976-1987 in the four main Dublin maternity hospitals are being traced and interviewed in order to obtain data for five main studies on NTDs:

1. A study of the risk of recurrence for NTD for all mothers who gave birth to an affected baby in the Dublin maternity hospitals during 1976-1987 and an examination of the factors influencing the recurrence risks; age, parity, social class, past obstetric history, type of NTD, hospital attended, periconceptional vitamin supplementation, time period.
2. A comparative study of clinical trial participants and non-participants, based on all mothers who had a baby with an NTD in the Dublin maternity hospitals during 1976-87, with particular emphasis on the recurrence rate of NTD and on the factors influencing the risk of recurrence.
3. A follow-up study of the mothers who participated in the trial to determine the recurrence rate in pregnancies subsequent to the trial and to check for possible side-effects of the trial treatments in the mothers and in the study babies.
4. A study of the survival rates and levels of handicap in the complete cohort of babies born with spina bifida in the Dublin maternity hospitals during 1976-1987.
5. A study, based on the cohort of spina bifida babies described at (4) above, of the medical care already received by the spina bifida children; the needs of the spina bifida children and their families for health and social services and the extent to which their needs are being met; and the impact (health, social, psychological, economic) on the family of caring for a member with spina bifida.

Study 1 above will provide essential information for accurate genetic counselling in an Irish population. The health services research studies described at 4 and 5 above will furnish useful information for those who plan and provide services for spina bifida children and will give much needed insight into the impact of spina bifida on the affected child, the family and the health and social services. In addition, topics 1-3 (especially number 2) will provide essential background information for the interpretation of the results of the trial. The data collected on this large group of NTD cases would also make it possible to conduct other epidemiological studies of NTDs.

The fieldwork for the follow-up study is being organised and coordinated by Anne Cleary, M.Soc.Sc. Interviewing commenced in August, 1989 and is scheduled to be completed in April, 1990. Data analysis will proceed during 1990 and publication of the findings of these studies is expected from 1991.

Maternal serum folate and vitamin B_{12} levels in pregnancies associated with neural tube defects.

The Health Research Board has been collaborating with the Department of Clinical Medicine and Biochemistry in Trinity College, Dublin and the Department of Clinical Microbiology in University College, Dublin, in a project examining maternal serum folate and vitamin B_{12} levels in women who give birth to infants with NTDs and in women with unaffected pregnancies. The study is based on serum samples collected during 1984-86 in four Dublin maternity hospitals (Coombe, National Maternity, Rotunda and St. James's) from women in early pregnancy as a routine rubella antibody screen.

To facilitate the completion of the other NTD studies data analysis in respect of this project has been postponed.

A prospective study of maternal blood levels of selected nutrients in pregnancies affected by neural tube defects.

The Health Research Board is collaborating with the Departments of Clinical Medicine and Biochemistry in Trinity College, the Department of Community Medicine and Epidemiology in University College, Dublin and the Coombe, National Maternity and Rotunda Hospitals in a

major prospective study of maternal blood levels of selected nutrients in pregnancies affected by NTD. The purpose of the study is to see if there are any important differences in early pregnancy maternal blood levels of selected nutrients between affected and unaffected pregnancies. Blood sample collection is scheduled to end in March, 1990.

An epidemiological study of orchidopexy (surgical operation for undescended testis) in Ireland.
(With Prof. B. O'Donnell, Our Lady's Hospital, Crumlin).
Preliminary results from this health services research/epidemiological study based on H.I.P.E. data suggest that the rate (per 100,000 boys aged 0-14 years) of this operation in Ireland increased markedly between 1978 and 1985 with differences in trends between Dublin and other areas of the country. The findings will be submitted for publication in 1990.

EC project on methods of identifying and recording occupational morbidity and mortality.
The EC working party on occupational and industrial history in cancer patients is investigating how to establish a system to identify and monitor occupational hazards in EC countries. Dr. P. Kirke and Dr. B. Herity are the Irish representatives on this working party. The working party has developed a questionnaire and has used an abbreviated set of coding instructions to ascertain subjects' occupational and industrial classification. Two phases of the project have been completed and Phase 3 is now underway.

The aim of Phase 3 is to explore the feasibility and potential difficulties of undertaking case-control studies using a standardised questionnaire in EC member countries. The questionnaire will be administered to 90 male patients in the age range 25 to 70 years in each country. The rationale for the case-control design of the study is to ascertain whether case-control studies would be sensitive enough to identify well established occupational hazards. The cases will be 25 patients with lung cancer and 30 patients with cancer of the haematopoietic system. The controls suggested for the study are 35 patients with stomach, colon or rectal cancer which have rarely been ascribed to an association with occupational hazards. All these cancers are highly prevalent. The main element of the analysis will be to assess odds ratios for each type of cancer in relation to known industrial hazards as reported in the literature for lung cancer and cancer of the haematopoietic system.

(d) Travellers Health Status Study
Dr. J. Barry, MRCP, MFCMI.
Health Research Board.
"Vital Statistics of Travelling People, 1987", the second report of the Travellers Health Status Study, was published in December 1989.[4] The report deals with fertility and mortality of Travellers.

Fertility of Travellers (Total births for 1987 = 565)
Traveller fertility is considerably in excess of fertility of settled people. The crude birth rate for Travellers is 35 per 1,000, as opposed to 17 per 1,000 of Irish people as a whole. The total fertility rate for Travellers is 5.3, as opposed to 2.3 for Irish women. Within the Travelling community fertility is over twice as high in those Travellers not living in houses during 1987.

Table 2.
Mortality in early life for Travellers in Ireland, 1987

	Ireland	Travellers *(95% confidence interval)*
Stillbirth Rate (per 1,000 total births)	6.9	19.5 (12.6 to 26.4)
Perinatal Mortality Rate (per 1,000 total births)	9.9	28.3 (20.0 to 36.6)
Infant Mortality Rate (per 1,000 live births)	7.4	18.1 (10.9 to 25.3)

Mortality of Travellers (Total deaths for 1987 = 95)

Indices of mortality in early life for Travellers are over 2½ times greater for Travellers than settled people (see accompanying Table 2).

The method used to measure overall mortality was indirect standardisation, the Standardised Mortality Ratio (SMR). For all causes of death the SMR was doubled for Travellers. The SMR for accidents (450) was twice as great as the SMR for natural causes (227). When Travellers currently living in houses were compared with those not in houses, the natural cause SMR was found to be the same but the accident SMR for those in caravans was over six times greater than for those in houses, 843 as opposed to 135. These results are summarised in Table 3.

Life expectancy for male Travellers is 10 years less at birth than for settled males and 12 years less for female Travellers than for settled females.

Data collection for the third report, which concentrates on postnatal and one year follow up of the babies born in 1987 continued in 1989. A feature of the follow up has been the mobility of Travellers in the first year of life, even among those Travellers who gave a home as their address at the time of birth.

(e) EUROCAT

Dr. A. Radic, MB,FFCMI.
Health Research Board.

EUROCAT is an acronym for an EC concerted action project for the epidemiologic surveillance of congenital anomalies. The analysis of the results of surveillance of congenital anomalies in the Eastern Health Board Area during 1980 - 1987 is in progress. The table below shows trends of selected malformations during that period. (See Table 4).

There are two items of special interest in the table. First shows the falling rates of neural tube defects (anencephaly, iniencephaly, encephalocoële, and spina bifida with or without hydrocephalus). This trend has been documented before from 1979 - 1984 and still continues. The decreasing trend was not confined to any subgroup of the population as defined by mother's age parity or socio-economic status.

Table 3

Standardised Mortality Ratios (SMRs) for Travellers, Housed and Unhoused, 1987

(Standard Population in Ireland)

	Irish SMR	SMR Housed Travellers (95% confidence interval)	SMR Unhoused Travellers (95% confidence interval)
All Causes (ICD 001-999)	100	218 (160 to 291)	317 (224 to 435)
Natural Causes (ICD 001-799)	100	228 (165 to 307)	225 (143 to 338)
Accidents (ICD 800-999)	100	135 (28 to 295)	843 (472 to 1,390)

Table 4

Prevelance at birth of selected congenital anomalies per 10,000 Total Births

1980 - 1987

Malformation	1980	1981	1982	1983	1984	1985	1986	1987
Neural Tube Defects	47.2	40.2	40.0	34.2	29.8	27.2	24.3	23.1
Congenital Heart Disease	42.7	50.9	46.5	51.0	61.4	63.7	62.5	57.4
Cleft Lip and/or Palate	15.6	20.1	16.3	18.2	14.2	13.1	14.9	16.7
Tracheo-Oesophageal Fistula with or without Oesophageal Atresia	4.6	3.9	4.1	2.6	2.7	4.2	2.4	3.9
Renal Agenesis and Dysgenesis	4.2	4.3	2.0	7.8	5.5	8.0	5.1	6.4
Congential Dislocation of Hips	19.1	30.4	31.0	27.3	49.0	31.4	26.1	30.9
Down's Syndrome	19.8	17.4	17.5	16.0	17.9	23.9	17.7	15.2

The second item of interest is the increase in rates of congenital heart disease, renal agenesis and dysgenesis and Down's Syndrome in 1985. These rates dropped the next year. These increases did not reach a statistical significance, but as they occurred in the same year and all three are at least partly subject to environmental factors it could be argued that some adverse environmental factors were abroad in 1984–1985 causing the increase.

Detailed analysis of other congenital anomalies is continuing.

Responsibility for maintaining the Dublin register of EUROCAT was transferred from the Board to the Eastern Health Board in October 1989.

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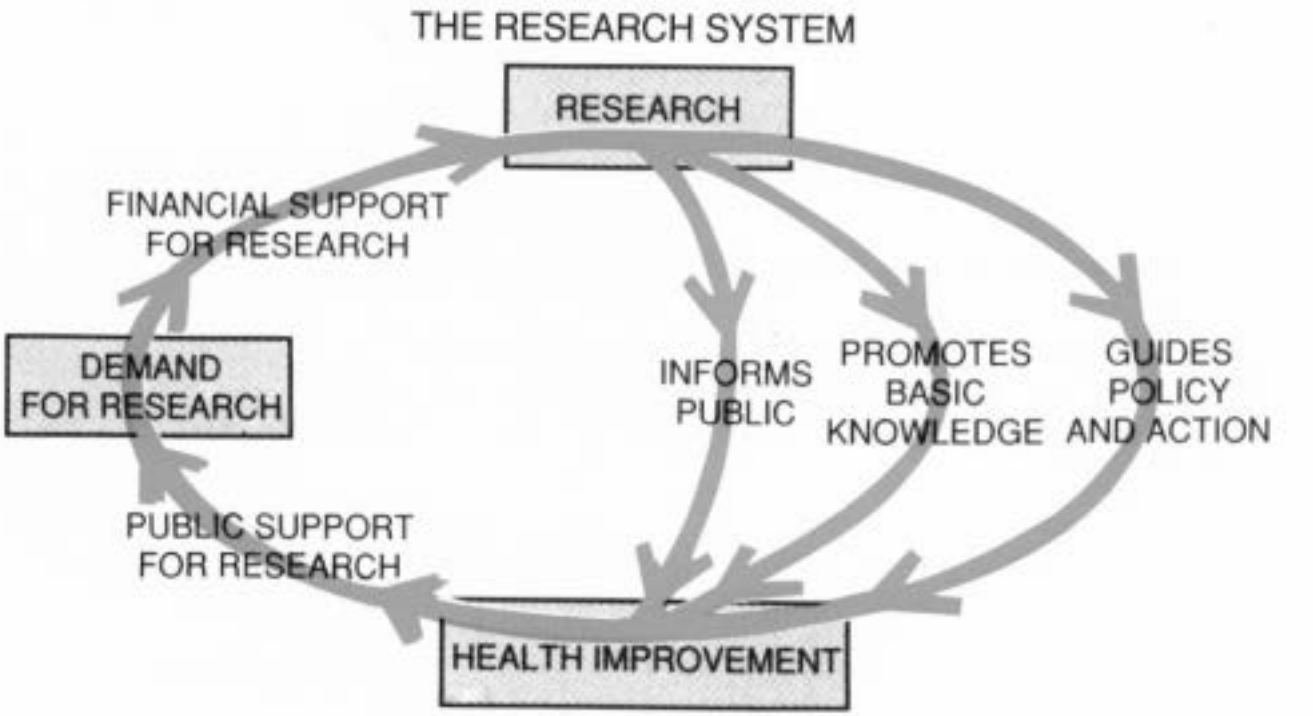

RESEARCH LABORATORIES

The research underway in the HRB funded laboratories located at Trinity College, focusses principally on the development of anti-cancer and anti-leprosy drugs and on virology studies. In 1989 work on the following projects was continued:

Title:

Molecular Combinations of Anti-Cancer Drugs (5-Fluorouracil and Nitrosoureas)

Project Leader:

Dr. R. S. McElhinney and Dr. J. E. McCormick in collaboration with Mr. C. M. Lucey

Summary

Alkylative cross-linking of complementary strands of DNA is a principal mode of cytotoxic action of N-(2-chloroethyl)-N-nitrosoureas (CNUs), and our synthetic programme is increasingly aimed at improving this by combining N-substitutes which would give longer cross-links than the two-carbon ethylene group (arising from the 2-chloroethyl compounds) with the very effective 5-FU-containing carrier moieties discovered earlier.

In addition to these symmetrical bis (NU's) we have also successfully achieved regiospecific location of two N-nitroso groups in molecules with four dissimilar area NH's. The effect of the resulting (unsymmetrical) complex molecular combinations, incorporating both CNU and MNU (N-methly-N-nitrosourea) fragments, on a repair enzyme of DNA metabolism is being investigated.

Cross-linking and pharmacokinetic studies with some of these very active drugs are being actively pursued in collaboration with laboratories in Europe and the U.S.

Title:

Dihydropyridine Calcium Modulators

Project Leader:

Dr. C. N. O'Callaghan

Summary

The object of this work is to prepare new dihydropyridine calcium modulators based on clinically active dihydropyridine agents e.g. the antihypertensives Nifedipine and Nitrendipine, the cerebral vasodilator Nicardipine etc.

Several potential calcium modulators have been synthesised, including some novel bridged tricyclic perhydropyridine products. In the course of preparing 'slow-realease' forms of the active 1,4-dihydropyridines, a unique series of 3,3-disubstitued tetrahydropyridines was obtained, and this has now been isolated for pharmacological testing.

Title:

Studies of clofazimine analogues and antihypertensive agents

Project Leader:

Dr. J. Byrne

Summary

Mycobacterium avium

New clofazimine analogues were tested against four strains **Mycobacterium avium**, a pathogen of great importance in patients suffering from AIDS. Replacement of the chlorine in the p-position of the anilino and phenyl rings by bromine made no significant difference to the activity. The trichloro derivative where the additional chlorine atom is in the 7-position of the nucleus also retained good activity; however, the addition of a chlorine atom in the 7-position to the dibromo-compound (B4071) gave a compound with markedly poorer activity (B4092).

Mycobacterium kansasii

Two strains of this opportunistic mycobacterium which has also been reported as a pathogen in AIDS patients were tested against eight clofazimine analogues and showed activity at 2.5 ug/ml or less.

Antihypertensive agents

New dihydropyridines synthesised by Dr. O'Callaghan were examined for inhibition of induced contractions in strips of rat aorta using Nifedipine as reference compound. Indications of promising activity have been obtained.

Title:

Analogues of Clofazimine

Project Leader:

Dr. J. F. O'Sullivan

Summary

Collaborative work with the Hansen's Disease Research Centre at Carville, Louisiana has resulted in the design of a compound with greater activity than heretofore, against *M.leprae*. The compound (B4090) is less soluble in body fat than clofazimine and hence should give rise to less skin colouration than the original agent. It is also active against a clofazimine-resistant organism.

Compounds with excellent activity against *M. avium* have been identified *in vitro* and are now being screened *in vivi* by Dr. Gangadharam in Denver. These should prove useful in the treatment of the opportunistic infections which cause disseminated life threatening diseases in AIDS patients.

The wound healing and anti-inflammatory properties of

the agents are also being examined in number of centres.

Virology Studies

Title:

Dengue Viral Pathogenesis

Project Leader:

Dr. M.A. O'Sullivan in association with Dr. H. Killen.

Dr. Aideen O'Sullivan, HRB Laboratories, Trinity College at work on a Third World Collaborative Research Project relating to an analysis of dengue virus pathogenesis. This research is being funded under the EC Tropical Medicine research programme.

Summary

The purpose of this EC sponsored study is to investigate the pathogenic mechanisms in dengue viral infections by identifying infected cel types using in situ hybridization and immunocyto-chemistry.

Two collaborative experiments have been organized:

1) use of in situ hybridization for rapid diagnosis in suspected dengue haemorrhagic fever (Department of Medical Microbiology/Department of Paediatrics, University of Indonesia/Ministry of Technology Jakarta)
2) identification of infected cell types in experimentally infected monkeys and infected human blood and biopsy material (Department of Paediatrics, Mahidol University/Siriraj Hospital/Armed Forces Research Institute of Medical Science, Bangkok).

A computer search for sequence homology between dengue serotypes revealed only one homologous region of 32 bases. This sequence and its complement have been synthesised and cloned into the Gemini vector for use as a riboprobe. Sections from mouse brains infected with the four dengue serotypes, Chickungunya virus, Japanese encephalitis virus and PBS have been prepared to test the specificity of this probe. An amplified biotin detection method has been developed for in situ hybridization.

Growth comparison of 10 clinical isolates of dengue virus serotypes 1 and 2 has been made in the mosquito cell line C6/36. Growth of the more virulent isolates has been examined in non-differentiated and differentiated U937 and HL-60 cell lines and primary human blood cells under different differentiation growth conditions.

(b) Viral Teratogenesis with Dr. G. Atkins and Mr. M. Mabruk

The causative agent for Spina Bifida is not known. A mouse model system was tested to determine if pre-natal viral infection could result in analogue clinical defects in the mouse embryo. Infection with an attenuated mutant of an abortogenic strain of Semliki Forest virus, at a specific time post conception, resulted in damage to the neural tube including open neural tube defects. Analysis by in situ hybridization and immunocytochemistry indicated that this damage was indirect and was caused by viral infection of mesenchymal cells surrounding the developing neural tube.

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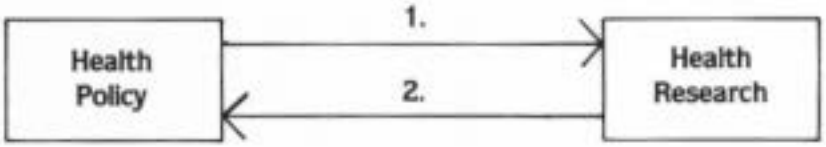
Relationship between Health Policy and Research



1. **To define relevant problems for Research**
2. **To utilize Research Results**

ACCOUNTS

Year Ended 31 December 1989

Income and Expenditure Account

	1989	1988
Income	IR£	IR£
Department of Health Grant	1,300,000	2,329,000
Interest Receivable	37,708	18,352
Other Income	176,348	63,773
Bequest		5,000
Externally Funded Research	211,706	238,213
	1,725,762	2,654,338
Expenditure		
General Research	512,912	484,022
Information Systems	169,839	465,372
Research Units	186,704	274,536
Laboratories at TCD	273,956	257,371
Epidemiological Studies	240,848	249,978
Externally Funded Research	211,706	238,213
Extra Mural Research		155,250
Administration	278,492	250,380
	1,874,457	2,375,122
(Deficit)/Surplus of Income over Expenditure for Year	(148,695)	279,216
Exceptional Item		
Profit on sale of Premises	445,008	–
Balance for Year	296,313	279,216

Balance Sheet

	1989	1988
Current Assets	IR£	IR£
Debtors and Prepayments	78,175	70,079
Monies on Deposit	665,131	179,000
Cash at Bank	38,673	244,186
Cash on Hand	25	10
	782,004	493,275
Current Liabilities		
Creditors and Accruals	98,643	110,808
	98,643	110,808
Net Current Assets	683,361	382,467
Investments	9,160	9,160
Fixed Assets	57,200	61,781
	749,721	453,408
Accumulated Fund		
Balance at 1st January	453,408	174,192
Balance for Year	296,313	279,216
At December 31	749,721	453,408

Auditor's Report

I have audited the accounts of the Health Research Board for 1989 in accordance with approved Auditing Standards. I have obtained all the information and explanations which I considered necessary.

In my opinion proper accounts and records are maintained and the financial statements give a true and fair view of the state of the Board's affairs as at 31st December 1989 and of its Income and Expenditure for the year then ended.

I have also issued a more detailed audit report to the Minister.

A. P. Doheny, F.C.A.
Local Government Auditor.

September 3, 1990

APPENDICES

APPENDIX A

The Executive of the Health Research Board

Chief Executive
Vivian O'Gorman, B.Sc., Ph.D.MICI., CChem., FRSC., MIWEM.

Secretary
John O'Gorman

Mental Health Studies
D. Walsh, MB., DPM., FFCM., FFCMI., FRC.Psych., FRCPI.

Mental Handicap Studies
D. Kavanagh, MRC.Psych.,DCH.

Congenital Abnormalities Register (EUROCAT) and Sudden Infant Death
A. Radic, MB.,FFCMI.

Perinatal and Child Health Studies
P. Kirke, MB.,FFCMI., FFCM., M.Sc., DCH., D.Obst.

Sociologists
A. O'Hare, M.Soc.Sc. (Senior Sociologist)*
H. Burke, B.Soc.Sc.
A. Cleary, M.Soc.Sc.
A. O'Connor, M.Soc.Sc **(Senior Sociologist)****
A. Kelleher, B.Soc.Sc.

*Until February 1989
**From March 1989

APPENDIX B

Special Committees of the Board –1989

Gastroenterology
Dr. G. H. Tomkin, *Chairman*, Professor F. Given, Professor M. Harrington, Dr. N. Keeling, Dr. J. Lennon, Dr. D. O'Donoghue, Professor J. Sheehan, Dr. M. Whelton, Dr. D. Headon, *Secretary*.

Haematology
Professor J. Scott, *Chairman*, Dr. T. G. Brien, Dr. P. Cotter, Dr. E. Lawlor, Dr. L.G. O'Connell, Prof. I. Temperley, Dr. T.J. Walsh, Dr. S.R. McCann, *Secretary*.

Immunology and Pathology
Professor C. F. McCarthy, *Chairman*, Dr. B. Bresnihan, Dr. J. K. Collins, Dr. C. Feighery, Professor J. F. Greally, Professor D. O'B. Hourihane, Dr. S. Kirrane, Dr. D. Reen, Dr. M.P.G. Little, *Secretary*.

Cancer
Professor K. O'Malley, *Chairman*, Professor D. Boucher-Hayes, Dr. P. Daly, Dr. P.P.A. Dervan, Professor H.F. Given, Dr. M.A. Hurley, Dr. D. McConnell, Dr. H. McLaughlin, Dr. M. Moriarty, Dr. H. Smyth, Dr. E. L. Egan, *Secretary*.

Cardiovascular Diseases
Professor K. O'Malley, *Chairman*, Professor G. Bourke, Dr. K. Daly, Dr. W. Fennell, Mr. V.P. Lynch, Dr. E.T. O'Brien, Mr G. Shanik, Dr. M.J. Walsh, Professor J. Feely, *Secretary*.

Mental Health and Neurology
Professor M. Webb, *Chairman*, Dr. A.G. Carroll, Dr. J. Dinn, Professor T. Fahy, Professor B.E. Leonard, Dr. S.D. McGrath, Dr. H. Staunton, Dr. J.L. Waddington, Dr. J.J. Cullen, *Secretary*.

Metabolism and Endocrinology
Professor J. Scott, *Chairman*, Dr. J. Finucane, Professor J.W. Hall, Professor J.J.A. Heffron, Dr. J. O'Donnell, Professor R.G. O'Regan, Professor D. Powell, Porfessor K.F. Tipton, Dr. H. Walsh, Professor M.P. Ryan, *Secretary*.

Microbiology
Professor M.X. FitzGerald, *Chairman*, Professor S. Condon, Prof. M. Clynes, Professor S. Doonan, Professor L.K. Dunican, Professor J. Flynn, Dr. R. Hone, Professor C.T. Keane, *Secretary*.

Pregnancy and Congenital Deformities
Professor G. Bourke, *Chairman*, Dr. R. Counahan, Dr. J. Gillen, Professor R.F. Harrison, Professor D.M Jenkins, Dr. P. Kelehan, Dr. D. Lillis, Dr. S. McManus, Dr. T.G. Matthew, Dr. C. Carroll, *Secretary*.

Respiratory Diseases
Professor M.X. Fitzgerald, *Chairman*, Dr. C.P. Bredin, Dr. L.J. Clancy, Dr. P. Finnegan, Dr. S. O'Neill, Dr. T.H. Peirce, Professor J. Prichard, Mr. A. Wood.

HRB Science Degree Scholarships
Professor K. O'Malley, *Chairman*
Professor R.G. O'Regan, U.C.D.
Professor J. Fraher, U.C.C.
Professor D.J. O'Donovan, U.C.G.
Dr. W. Clayton Love, T.C.D.
Dr. C. Buckley, R.C.S.I.

APPENDIX C

Health Research Board Representation on International Committees

Commission of the European Communities

Management & Co-ordination Advisory Committee in Medical & Health Research (CGC)
Dr. T. O'Dwyer, Department of Health, Hawkins House, Dublin 1.
Professor K. O'Malley, Royal College of Surgeons in Ireland, Dublin 2.

COMACS (Concerted Action Groups) of CGC

Epidemiology
Dr. M. Wiley, Department of Health, Hawkins House, Dublin 2.
Professor G. Bourke, University College, Dublin 2.

Bioengineering
Professor C.T. Doyle, University College, Cork.
Professor S.M. Lavelle, University College, Galway.

Medical Biology
Professor G.H. Tomkin, 1 Fitzwilliam Square, Dublin 2.
Professor C.F. McCarthy, University College, Galway.

Health Services Research
Mr. D. Doherty, Midland Health Board, Tullamore, Co. Offaly.

EEC Programme on Medicine, Health & Nutrition in the Tropics
Professor J. Scott, Trinity College, Dublin 2.
Dr. H.P. Voorheis, Trinity College, Dublin 2.

EEC Working Party on Medical & Health Research concerning Drugs (COST)
Professor J. Feely, Trinity College, Dublin 2.

EEC Programme on Advanced Informatics in Medicine (AIM)
Dr. V. O'Gorman*

EEC Working Party on Identification and Recording of Occupational Morbidity and Mortality
Dr. P. Kirke*

EEC Concerted Action for Epidemiological Surveillance of Congenital Anomalies. Project Management Group
Dr. A. Radic*

EEC Working Party on Delivery of Health Care to the Elderly
Dr. D. Walsh*

EEC Working Party on Dementia
Dr. D. Walsh*

EEC Directorate General 5E1, Cocaine Steering Group
Mrs. A. O'Hare*

European Science Foundation (ESF)

European Medical Research Council (EMRC) – A Sub committee of the ESF
Professor J. Scott, Trinity College, Dublin 2.

EMRC Study Group on Mental Illness Research
Professor M. Webb, St. Patrick's Hospital, James's Street, Dublin 8.

ESF Programme of Fellowships in Toxicology (PGT)
Professor J. Feely, Trinity College, Dublin 2.
Professor K. O'Malley, Royal College of Surgeons in Ireland, Dublin 2.

ESF European Training Programme (ETP) in Brain & Behaviour Research
Professor B.E. Leonard, University College, Galway.

World Health Organisation (W.H.O.)

W.H.O. European Advisory Committee on Health Research
Dr. M. Wiley, Department of Health, Hawkins House, Dublin 2.

W.H.O. Expert Committee on Mental Health
Dr. D. Walsh*

Council of Europe

Epidemiology Sub Group (Pompidou Group)
Mrs. A. O'Hare*

* Health Research Board
73 Lower Baggot Street,
Dublin 2.

APPENDIX D

Health Research Board Representation on National Committees

National Health Council

Professor G.H. Tomkin, 1 Fitzwilliam Square, Dublin 2.

Ms. M. Dwyer, City of Dublin Skin and Cancer Hospital, Dublin 2.

Royal Irish Academy National Committee for Chemistry

Dr. J.F. O'Sullivan, H.R.B. Laboratories, Trinity College, Dublin 2.

Royal Irish Academy National Committee for Nutritional Sciences

Dr. M.J. Gibney, Trinity College, Dublin 2.

Kilkenny Health Project

Representatives on Board of Directors:
Dr. T. O'Dwyer , Mr. J. O'Gorman*

Representatives on Finance Committee:
Mr. J. O'Gorman*

Representatives on Scientific Committee:
Dr. A. Radic*

Travellers Health Status Project

Representatives on Advisory Committee:
Mr. J. O'Gorman*

Representatives on Scientific Committee:
Dr. P. Kirke*, Dr. J. Barry*

* Health Research Board,
73 Lower Baggot Street,
Dublin 2.

APPENDIX E

Publications 1989

Barry, J., Herity, B. and Solan, J. The Travellers' Health Status Study: Vital Statistics of Travelling People, 1987. The Health Research Board, Dublin, 1989.

HRB News Number 1. The Health Research Board, Dublin, March 1989.

HRB News Number 2. The Health Research Board, Dublin, July 1989.

O'Connor, A. and Walsh, D. Activities of Irish Psychiatric Hospitals and Units 1986. The Health Research Board, Dublin, 1989.

O'Connor, A and Walsh, D. Activities of Irish Psychiatric Hospitals and Units 1987. The Health Research Board, Dublin, 1989.

Research Summaries: Compendium of Completed Research Projects 1987-1988. The Health Research Board, Dublin, 1989.

Research Unit Report No. 1: Drugs in the Elderly. The Health Research Board Dublin, September 1989.

APPENDIX F

Research Projects approved by HRB in 1989

Dr. J. E. Gillan, *Histopathology, Rotunda Hospital.*
"The pathology of the placenta in sudden infant death syndrome – a search towards prevention".

Dr. S. Thompson *and* Dr. J. F. Atkins, *Genetics, TCD; Biochemistry, UCC.*
"Translational frameshifting influenced by an antibiotic".

Professor G.H. Tomkin, *Diabetes, Adelaide Hospital.*
"Lipoprotein alterations in diabetes".

Dr. S. Ennis, *Phsyiology, UCD.*
"Scanning electromicroscopy of retinal vasculature in diabetic rats".

Dr. P.A. Carney, *Psychiatry, University College Hospital, Galway.*
"Melatonin in affective disorders".

Dr. A.V. Stanton, *Pharmacology, UCD.*
"The relationship between blood pressure level, salt and fluid balance, and natriuretic factor".

Professor A.J. Cunningham, *Anaesthesia, Beaumont Hospital.*
"Adrenoceptor and neuroendocrine responses to aortic cross clamping and release during abdominal aortic surgery.

Dr. J. Jackson, *Immunology, St. James's Hospital.*
"Functional properties of C1-inhibitor in health and disease.

Professor M.P. Ryan, *Pharmacology, UCD.*
"The effects of cardiovascular drugs on ion transport in experimental models of cardiac ischaemia".

Dr. F.R. Falkiner and Dr. E.A. Kiely, *Clinical Microbiology, St. James's Hospital; Genitourinary, Meath Hospital.*
"Bacterial causes of infective complications of transurethal resection of the prostate".

Dr. C.J. Smyth, *Microbiology, TCD.*
"Pathogenesis of *Campylobacter pylori* infection".

Dr. M.A. De Arce, *Genetics, TCD*
"Modification of prior risks for potential carriers of cystic fibrosis (C.F.) using DNA markers in linkage disequilibrium with the CF gene; data for Ireland".

Prof. C. O'Herlihy, *National Maternity Hospital, Holles Street*
"Clinico-epidemiological study of cerebral palsy".

Dr. M. Fitzgerald, *Child and Family Centre, Eastern Health Board.*
"Prevalence of child psychiatric disorders in an Irish urban area".