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Pharmaceutical Research in Plymouth

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The Hospital Pharmacist

PHARMACEUTICAL RESEARCH IN PLYMOUTH

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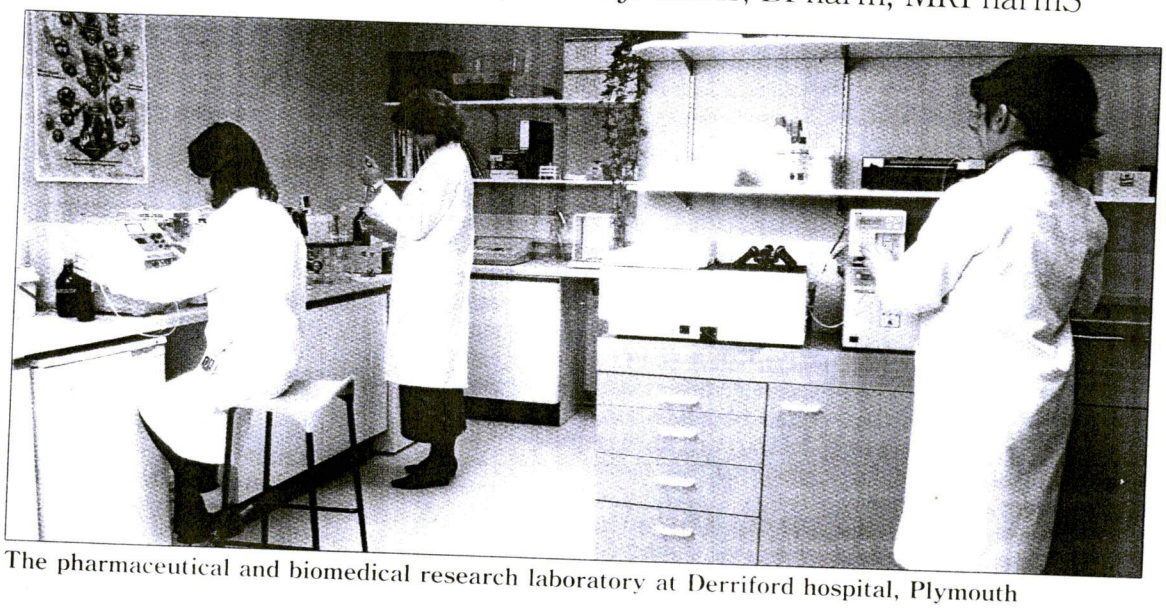

Pictures: Magnus Rea

The pharmaceutical and biomedical research laboratory at Derriford hospital, Plymouth

WITH over 1,350 beds covering all major specialties, including a Calman cancer centre, Plymouth's Derriford hospital is one of Europe's largest and most active non-teaching hospitals. Recognising the need to respond to clinical and academic developments in the hospital, the director of pharmacy has actively encouraged the establishment of a strong research culture within the pharmacy department. This process began with the appointment of clinical trials and clinical audit pharmacists in 1991 and 1992, respectively. More recently, a research and technical services (RTS) manager was appointed. This position has a nominal 50 per cent time allocation for research work and, in a joint venture with the University of Plymouth, is combined with the academic appointment of reader in biomedical sciences at the Plymouth postgraduate medical school.

In January, 1996, a postdoctoral research scientist was appointed and a pharmaceutical and biomedical research laboratory was established within the pharmacy department. As a result of these developments, the current research activities of the pharmacy department include clinical audit, pharmaceutical and biomedical research, clinical research, practice research and pharmacoeconomic research.

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Research activities within the pharmacy department at Derriford hospital, Plymouth, have improved patient care, reduced treatment costs, attracted external funding and have brought recognition to the department

The key research responsibilities of the RTS manager can be summarised as:

1. Developing personal research interests which are of relevance to the pharmacy department and/or Plymouth Hospitals NHS trust.
2. Directing postgraduate research projects.
3. Co-ordinating and developing research ideas within the pharmacy department.
4. Providing guidance on the acquisition of research funding, experimental design, data analysis and publication of research.
5. Contributing to the academic output of the Plymouth postgraduate medical school.
6. Establishing collaborative research with industry, academia and healthcare professionals. The RTS manager also has postgraduate teaching and course development responsibilities associated with his university appointment. However, in the pharmacy department, education and training, and the supervision of clinical diploma students, is primarily the responsibility of the clinical pharmacy manager.

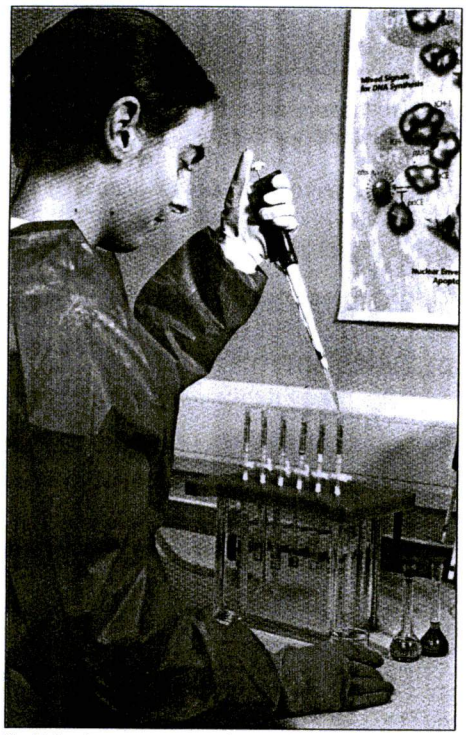
RESEARCH FACILITIES

The pharmacy's pharmaceutical and biomedical research laboratory is equipped for studies on drug formulation, drug stability, clinical pharmacokinetics and the evaluation of drug delivery systems. The development of a joint research project with the haematology department has also provided access to cell-culture and flow-cytometry facilities, which are used to characterise malignant cells following drug treatment. Specialised techniques, including scanning electron microscopy, are available on the main university campus.

Office accommodation for clinical trials, practice research, biomedical research and clinical audit, is equipped with a fully networked computer system, which has internet access and on-line search capability. Specialist software packages in graphics, statistics, pharmacokinetic modelling and literature management are also available to researchers.

CLINICAL AUDIT

The concept of clinical audit is well accepted in the pharmacy department, having developed progressively over the past



Solid-phase extraction of drugs and metabolites within the research laboratory

four years. Clinical audit is considered here as a research activity, partly because of its interaction with other research functions (pharmacoeconomics, clinical research), and also because recommendations and solutions to problems often arise as a result of audit. An agreed programme of clinical audit is set out at the beginning of each year and is included in the pharmacy business plan. Clinical audit is led by a clinical audit pharmacist ("D" grade), who is supported by other pharmacists within the department, many of whom have attended a training workshop on the principles and practice of clinical audit.

Many in-house pharmacy operational issues have been addressed through audit. An audit of the pharmaceutical aspects of the patient discharge process has resulted in recommendations being made to overcome difficulties affecting the delivery of an accurate and timely service to the wards. The implementation of changes in work routine within the dispensary, and at ward level, has resulted in a more efficient and patient-focused service. Another project involved the destruction of patients' own medication, the problem having been raised by primary care colleagues. An audit of the appropriate handling of patients' own medication has enabled ward staff to adopt a more structured approach.

Outside of the pharmacy department, the approach to clinical audit is multidisciplinary, with the focus on promoting clinical effectiveness and improved patient outcomes. Many topics are prompted by a close relationship with clinical directorates and pharmacy involvement in the management of directorate budgets. Drug audit is particularly directed at areas where changes in prescribing practice can be achieved, where high cost drugs are prescribed, or where new drugs are added to the hospital formulary. For example, the dramatic increase in the prescribing of isotretinoin for acne, and the introduction of starch-based plasma expanders on the intensive care unit, have prompted clinical audit projects.

A clinical audit project undertaken jointly with the surgical directorate on the administration of prophylactic subcutaneous heparin to general surgical patients achieved second place in the Plymouth Hospitals NHS trust clinical audit competition for 1996. Routine assessment and appropriate management of thromboembolism for all general surgical patients is now recorded as standard practice at admission. An increasing proportion of patients receive their first dose of prophylactic subcutaneous heparin preoperatively as recommended from the results of the audit. An audit on the current prescribing practice and knowledge of oral anticoagulation has recently been completed as part of a Master of Science degree project. In-house guidelines on the best practice for treatment and management of this group of patients have been produced in conjunction with the haematology department. A commitment by our clinical pharmacists to ensure pre-discharge patient counselling, and improvement of communication with primary care colleagues, will improve the transfer of care of the patient into the community.

RESEARCH

Pharmaceutical and biomedical research encompasses a wide range of inter-related pharmaceutical sciences, including drug formulation, stability and compatibility studies, bioanalytical work and the development of pharmacokinetic/pharmacodynamic (pk/pd) models for dose optimisation. Research of this type can be applied throughout the therapeutic spectrum, although cancer chemotherapy and drug stability in ambulatory infusion devices are areas of particular interest in Plymouth. More recently, the research group has developed an interest in the interaction between cytokines and cytotoxic drugs at the cellular level,[1] with the aim of rationalising multiple-agent chemotherapy and overcoming drug resistance.

Pharmaceutical and biomedical research is carried out under the direction of the RTS manager, with support from the post-doctoral research scientist. Two externally funded postgraduate students are currently engaged in full-time biomedical research and are registered with the postgraduate medical school, University of Plymouth, for the degree of PhD. Access to the research laboratory is also open to other members of the pharmacy staff to enable them to undertake specific research projects.

One of the PhD research projects is concerned with the development of pk/pd relationships for a central nervous system-acting drug with therapeutic applications in Parkinson's disease. The aim of this project is the optimisation of drug dosage for individual patients to maximise efficacy and minimise toxicity. This involves the development of an ultrasensitive liquid chromatography assay for the drug and its metabolites in plasma, and complex pharmacokinetic modelling techniques to analyse data from both conventional and novel drug delivery systems. The research student is required to work closely with patients and clinicians to evaluate pharmacodynamic responses to the drug, an aspect of the research which helps to re-inforce the clinical significance of this study.

The second PhD project is concerned with the effect of cytokine modulation of the multidrug resistant mdr-1 phenotype on apoptosis (programmed cell death), induced by anthracycline drugs in B-type chronic lymphocytic leukaemia (B-CLL). This is a collaborative project with the department of haematology and uses cell culture and flow-cytometry techniques to determine mdr-1 functionality, cell apoptosis and the anthracycline drug content of B-CLL cells. Further evaluation of intracellular drug and drug-metabolite concentrations will be carried out using capillary electrophoresis. This project will enhance our understanding of the complex interactions between cytokines, for example, alpha-interferon and interleukin II, and cytotoxic drugs, and will also provide information on the role of cytokines in reversing cancer cell drug resistance, often one of the main causes of treatment failure in cancer chemotherapy.

Often, research projects arise from discussions with clinical colleagues or originate from problems identified by ward pharmacists. The re-formulation of arachis oil-based fat soluble vitamin preparations to avoid nut allergies, and the development of dispersent solutions to convert tablet formulations of cytotoxic drugs to oral liquids for paediatric use, are two examples of this.

The pharmacy department has a strong interest in the provision of "hi-tech" healthcare for domiciliary patients. Developments in home infusion therapy have initiated stability and compatibility studies on a wide range of analgesic, antibiotic, antiviral, total parenteral nutrition and cytotoxic drug infusions. It is essential that home infusions are physically and chemically stable under prolonged refrigerated storage and transport conditions, and also under in-use conditions where a drug infusion delivered from an ambulatory pump (worn under the patient's clothing) may reach body temperature. Although most of these studies are focused on the needs of local home-care patients, a number of collaborative studies with the pharmaceutical, home-care and medical device industries are also undertaken on a regular basis.

With the planned relocation of the Plymouth cancer centre to Derriford hospital within the next year, much of the pharmaceutical and biomedical research planned for the immediate future is related to oncology and palliative care. This will include studies on the extended stability of cytotoxic drug infusions, pk/pd studies for dose and schedule individualisation, and the development of environmental monitoring techniques for the simultaneous determination of occupational exposure to multiple cytotoxic drugs. A major study on the compatibility of two- or three- drug admixtures in

syringes for palliative care is being piloted as a preregistration pharmacist project, and a joint grant application with the department of palliative medicine has been submitted to secure funding for longer term studies.

CLINICAL STUDIES

Since 1991, the pharmacy department has employed a pharmacist with specific responsibilities for the organisation and co-ordination of clinical trials. To achieve the directives of good clinical practice (GCP), the local research ethics committee directs all investigators to pharmacy for the co-ordination, dispensing, storage and accurate record keeping required.

The number of trials in progress has more than doubled in the past three years to some 64 (excluding haematology and oncology chemotherapy protocols that are current standard practice). The number of trials is set to continue increasing at the current rate of two, or more, per month as the research activity in Plymouth continues to increase.

Most of the current trials are pharmaceutical company-led phase III comparative or phase II placebo controlled studies, for which the pharmacy service is charged at a rate comparable to most other hospital pharmacies. However, the number of in-house clinical trials continues to increase. These are a particular challenge to the clinical trials pharmacist since the investigator often requires assistance with DDX (doctors' and dentists' exemption scheme) application, protocol design, submission to the local research ethics committee, randomisation, attainment of trial supplies, sponsorship, and blinding of packaging. In addition to these, there are several Medical Research Council (MRC) conducted clinical trials which, although requiring considerable pharmacist and dispensary input, are not funded for pharmacy services.

The majority of clinical directorates within the hospital trust are involved in clinical trials, with a third of the current studies being conducted within the directorate of clinical oncology. With the planned appointment of more medical staff to joint clinical and academic positions, a significant increase in the number of in-house and phase I and II studies conducted in Plymouth is expected. The challenges provided by these developments will be balanced by increased opportunity for the pharmacy department to become involved in the design and operation of clinical trials.

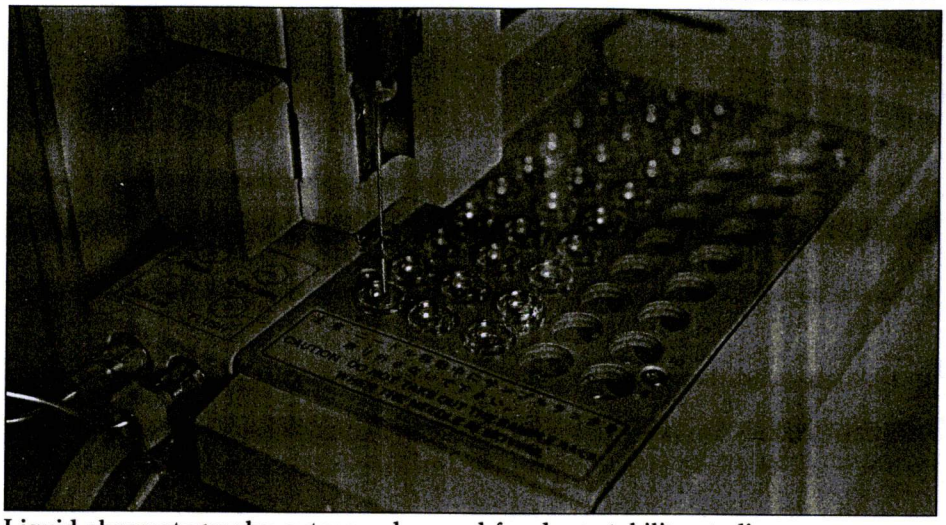
PRACTICE RESEARCH

Projects in practice research are often related to one or more of the key research interests described previously. For example, a study has recently commenced in Plymouth to evaluate the role of the hospital pharmacist as a facilitator in shared-care and "hi-tech" home-care initiatives. The project, which will run for two years, has received grant funding from the NHS Executive research and development directorate to support a research pharmacist on a full-time MPhil programme. Focused at the primary-secondary care interface, the aim of the project is to evaluate the effectiveness of hospital pharmacist input into the development and implementation of shared-care initiatives, and also into the development of "hi-tech" infusional treatments in the domiciliary setting. The research will also involve the development of financial models to quantify the cost of treatment options and will explore the funding issues which, unless resolved, can often preclude innovative approaches to patient care. Supervision of this project, which commenced in July, 1996, is shared between the research and technical services manager, the director of pharmacy and the community services manager. Collaboration with colleagues in the primary care and health authorities sectors will be developed as the research progresses.

A pharmacist based at Derriford hospital has recently completed a study to determine the information needs of patients receiving chemotherapy and their general practitioners.[2] This work has resulted in the development and printing of information packages for patients and GPs. The patient information package contains general information on chemotherapy and a set of information cards (one for each drug), so that patients can receive specific information on the drugs used in their treatment regimen.

Further research enabled "fine-tuning"of the style, content and presentation of the package. The GP information package contains general information on the management of late side effects of chemotherapy and a "data card" for each cytotoxic drug, providing specific details on the mode of action, precautions in use, adverse effects and any special instructions. Follow-up research established the acceptability of these packages to patients, oncologists, oncology nurse specialists and GPs.

Pharmacoeconomic studies are an important area of practice research in Plymouth. Current studies, initiated by the purchase and formulary manager, include an evaluation of the dose and scheduling of $5HT_3$ antagonists in oncology antiemetic protocols and the selection of first-line antimicrobial therapy for immunocompromised patients on the haematology ward.



Liquid chromatography autosampler used for drug stability studies

CONCLUSION

With many competing demands on time and resources, pharmaceutical research in the hospital setting can be a difficult proposition. Success demands a strong commitment to research from pharmacy managers, and staff involved in research must be prepared to work in their own time. For those prepared to accept the challenge, the clinical objectives of hospital research, combined with the close proximity of patients and clinical colleagues, can provide one of the most rewarding research environments imaginable. The integration of research activities and full-time research students into the pharmacy department has helped to stimulate a research culture and encourages staff to take a more critical and reflective approach to their every-day practice.

The research portfolio of the pharmacy department at Derriford hospital is unusual in both its diversity and its inclusion of research areas, such as biomedical research, which are normally restricted to academia. This approach caters for a wide range of research interests and has provided exceptional opportunities to contribute to collaborative research.

Our experience has shown that research can improve patient care, improve practice, reduce treatment costs, attract external funding and bring recognition to the department. For the individual, pharmacist or scientist, the opportunities provided by research in terms of personal and professional development are unlimited.

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