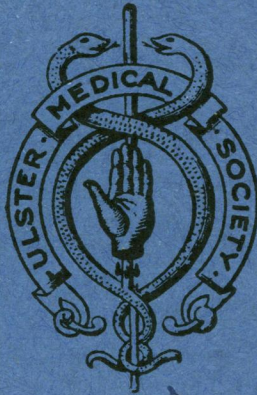


VOLUME 53

1984

No. 1

# THE ULSTER MEDICAL JOURNAL



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# CONTENTS

	<i>Page</i>
THE ROYAL MATERNITY HOSPITAL, BELFAST — FIFTY GLORIOUS YEARS 1933-1983: J McD G Harley - - - - -	1
A HOSPITAL FOR ALL SEASONS: JA Weaver - - - - -	18
A RECIPE FOR TRANSPLANTATION: Mary G McGeown - - - - -	33
PRIMARY SCLEROSING CHOLANGITIS: RAJ Spence, JR Anderson, GW Johnston, TT Fulton, ME Callender - - - - -	44
ROUTINE MEASUREMENT OF HAEMOGLOBIN A <sub>1</sub> AT THE DIABETIC OUTPATIENT CLINIC: E Byrne, G Savage, JD Merrett, L Kennedy -	51
A STUDY OF 100 CONSECUTIVE REFERRALS IN A UNIVERSITY PSYCHIATRIC CLINIC: A Kerr - - - - -	58
OUTCOME OF PREGNANCY IN A RUBELLA OUTBREAK IN NORTHERN IRELAND 1978-1979: JH Connolly, NC Nevin, DM Simpson, HJ O'Neill - - - - -	65
UNSUSPECTED Q FEVER ENDOCARDITIS — A CASE REPORT: K Moles, ME Scott, H O'Kane, JH Connolly - - - - -	74
SCREENING FOR CERVICAL CANCER IN GENERAL PRACTICE: Maura Briscoe, J Oliver Woods - - - - -	76
HIGH FREQUENCY JET VENTILATION AND ASPIRIN POISONING: WI Campbell, DL Coppel, BF McLaughlin - - - - -	80
RECTOVAGINAL FISTULAE FOLLOWING RADIATION TREATMENT FOR CERVICAL CARCINOMA: JR Anderson, RAJ Spence, TG Parks, EB Bond, BD Burrows - - - - -	84
PRELIMINARY REPORT — SPORTS INJURY CLINIC: K Elizabeth Dowey -	88
CAREER PREFERENCE ENQUIRY AMONG QUEEN'S UNIVERSITY MEDICAL UNDERGRADUATES AND GRADUATES: STAGE III: Elizabeth A Egerton	93
BOOK REVIEWS - - - - -	98-102

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# C O N T E N T S

	<i>Page</i>
THE ROYAL MATERNITY HOSPITAL, BELFAST — FIFTY GLORIOUS YEARS 1933-1983: J McD G Harley - - - - -	1
A HOSPITAL FOR ALL SEASONS: JA Weaver - - - - -	18
A RECIPE FOR TRANSPLANTATION: Mary G McGeown - - - - -	33
PRIMARY SCLEROSING CHOLANGITIS: RAJ Spence, JR Anderson, GW Johnston, TT Fulton, ME Callender - - - - -	44
ROUTINE MEASUREMENT OF HAEMOGLOBIN A <sub>1</sub> AT THE DIABETIC OUTPATIENT CLINIC: E Byrne, G Savage, JD Merrett, L Kennedy -	51
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OUTCOME OF PREGNANCY IN A RUBELLA OUTBREAK IN NORTHERN IRELAND 1978-1979: JH Connolly, NC Nevin, DM Simpson, HJ O'Neill - - - - -	65
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SCREENING FOR CERVICAL CANCER IN GENERAL PRACTICE: Maura Briscoe, J Oliver Woods - - - - -	76
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PRELIMINARY REPORT — SPORTS INJURY CLINIC: K Elizabeth Dowey -	88
CAREER PREFERENCE ENQUIRY AMONG QUEEN'S UNIVERSITY MEDICAL UNDERGRADUATES AND GRADUATES: STAGE III: Elizabeth A Egerton	93
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# THE ULSTER MEDICAL JOURNAL

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3. The text should indicate the purpose of the paper, and should include an introduction, sections on materials and methods, results, and a discussion relevant to the findings. A brief factual summary should be provided.
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  - i) a list of all authors when six or less (when seven or more only the first three should be listed followed by *et al*).
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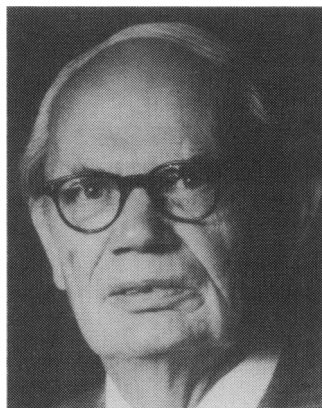
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**JOHN EDGAR MORISON**  
**Editor of the Ulster Medical Journal**  
**1952 - 1984**

For some time this Journal has published neither editorials nor obituaries, and neither is called for in this issue. But we cannot go to press without a comment to record the longest Editorship in the history of our Society. John Edgar Morison has held that office from 1952 to 1984 with distinction, efficiency and much affection.



The Ulster Medical Journal exists today as a strongly based local medical publication, recording annual orations and addresses by our senior colleagues, important local medical observations, and always supporting the tentative first steps of embryo authors. It exists because of local support and interest, both intellectual and financial. It has survived in a changing world because it is needed and because of the good quality of papers which have sought publication. But its present healthy state reflects the wise guidance and policy of the senior editor for over 30 years.

An editor does much more than accept or even refuse articles. He may wield great power with a blue pencil over the split infinitive or the passive voice. He encourages brevity of content and economy of words, he advises on layout and form, even for a presidential address. The Ulster Medical Journal survives, when many other local medical journals have disappeared, as a tribute to good editorial stewardship.

Good medical writing will survive into the age of the word processor only if the journal provides the right stimulus and its editorial team take the time and the trouble to advise and encourage the words latent in us all to flow freely but correctly on to the printed page. We will do our best to follow the high standards set.

*"Reading maketh a full man,  
conference a ready man,  
and writing an exact man"*

Francis Bacon (1561-1626)

## THE ULSTER MEDICAL SOCIETY

Whitla Medical Building  
97 Lisburn Road  
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If you are not a member of the Ulster Medical Society, we would appeal to you to give the question of joining your consideration. The Society has been in existence since 1862 (and is the direct descendant of the Belfast Medical Society founded in 1806), and has always been active in keeping its members interested in the advances in medical science. Meetings are held at intervals of a fortnight during the winter months, and papers are contributed by members and distinguished guests. Facilities are provided for doctors to meet informally afterwards, and have a cup of tea. *The Ulster Medical Journal, the official organ of the Society, is issued to all Fellows and Members free of charge.* The Society is now rehoused in its own Rooms and in the Whitla Medical Building of Queen's University at 97 Lisburn Road, and this replaces the Whitla Medical Institute which had to be vacated in 1965.

May we, therefore, appeal to you to join the Ulster Medical Society, and so enable us to widen its influence and sphere of usefulness still further? A proposal form is appended; your proposer and seconder must be Fellows of the Society. If you do not know any Fellows please contact the Honorary Secretary. All persons registered as medical practitioners under the Medical Act shall be eligible for election as members of the Society (Constitution, Section VI). Temporary membership may be allowed at the discretion of the Council.

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# THE ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

VOLUME 53

1984

No. 1

## **THE ROYAL MATERNITY HOSPITAL, BELFAST FIFTY GLORIOUS YEARS 1933-1983**

**PRESIDENTIAL ADDRESS TO THE ULSTER MEDICAL SOCIETY,  
20th October 1983**

by

**J. McD. G. HARLEY**

THE hospital from which the Royal Maternity evolved was conceived 140 years before at a meeting in the Linen Hall on 23rd December 1793 by a group of 180 ladies who called themselves "The Humane Female Society for the Relief of Lying-in-Women". After a short gestational period of 11 days the first Belfast Lying-in-Hospital was born on 4th January 1794. It was a house — No. 25 Donegall Street — rented for 12 guineas per annum and contained six beds. After 35 years, due to deplorable conditions, the hospital moved in August 1830 to Clifton Street opposite the Charitable Institution. Here it was to remain for 74 years before moving to Townsend Street where the new Incorporated Belfast Maternity Hospital was built with 26 beds. This hospital, later occupied by Melville Ltd, a firm of undertakers, was opened on 7th November 1904.

In 1907, that is three years after opening in Townsend Street, a Dr C.G. Lowry was appointed house surgeon. This is the first appearance of the name of this man who, more than any other, was responsible for the building of the present Royal Maternity. Interestingly, he applied unsuccessfully to join the staff in 1909. However, on the death of Professor Byers, Professor of Midwifery, Queen's University of Belfast, 1893-1920, he was appointed to the Chair of Midwifery and joined the staff. The Chair at that time was divided into two — Dr R.J. Johnston being appointed to a Chair in Gynaecology.

From 1925 onwards, Professor Lowry, with the help and encouragement of the then Professor of Medicine, James Lindsay, who was also Chairman of the Board of Governors of the maternity hospital, started a campaign to secure a site for a new maternity hospital in the proximity of, and amalgamated to, the Royal Victoria



Hospital. In 1926, at his own expense, Professor Lowry visited the most recently built hospitals in the USA and Canada. On his return, hearing that the Marquis of Dufferin and Ava was going to Canada, Professor Lowry invited him to visit Townsend Street Hospital to see for himself the problems, and advised the Marquis to visit those hospitals in Canada that he had seen. On returning, the Marquis interviewed by the Press, remarked, "Belfast should be ashamed of its City Hall". When the astonished reporters enquired why, Lord Dufferin replied, "A city that has a maternity hospital like Townsend Street and a City Hall such as it is, should be ashamed".

Professor Lowry's original proposal in 1926 for the amalgamation was turned down but subsequently passed on 6th May 1927 at a Special Meeting of the Board of Governors, which was held following the Annual General Meeting at which the Right Honorable John Milton Andrews, Minister of Labour and later Prime Minister, spoke strongly supporting the amalgamation with the Royal. The next step was to persuade the staff and members of the Board of Management of the Royal. To do so, Professors Lowry and Lindsay prepared a circular entitled "The Need for Better Maternity Accommodation for Belfast and Northern Ireland".

Some of the contents of the circular are important and here I quote Professor Lowry, "In the year 1925, 150 women in Northern Ireland died in pregnancy and childbirth (this represents one in 10 of all deaths in women between 20 and 45 years of age), that is, three women per week lose their lives in what is the exercise of their highest function. The public conscience is not sufficiently sensitive to the death rate in childbirth. If 150 women per annum lost their lives by some epidemic disease of unknown cause and with an unusual name, very serious note would be taken of it". He suggested the following remedies:

1. *Better and more ample hospital accommodation.* In this, Belfast was seriously behind, as you can see from these comparative figures, which show the population of eight leading centres and the number of beds available for midwifery. Belfast is bottom of the list.

	<i>Population</i>	<i>Beds</i>
Dublin	400,000 approx.	255
Glasgow	1,034,000	108
Edinburgh	420,000	104
Newcastle-on-Tyne	275,000	70
Cardiff	200,000	50
Leeds	548,000	50
Bradford	286,000	42
Belfast	414,000	26

2. *The provision of better educational facilities for students and nurses.* Again I quote, "... The modern hospital is not only a resort for the sick but an educational institution where the rising generation of students and nurses receive a training which will enable them in their turn to be of service to the community".

The Board of Governors of the Royal Victoria Hospital received the circular with an accompanying letter from William Leslie, the Secretary to the Incorporated Belfast Maternity Hospital, and after much discussion, finally, three months later, agreed on 28th September 1927 to amalgamation.

Having accomplished all this, the necessary measures were taken to plan the hospital and raise the money to build it. The original proposal was for 100 beds for obstetrics and 50 for gynaecology, the gynaecological unit of the RVH to be transferred to the new building. Fifty years on we still await this latter event.

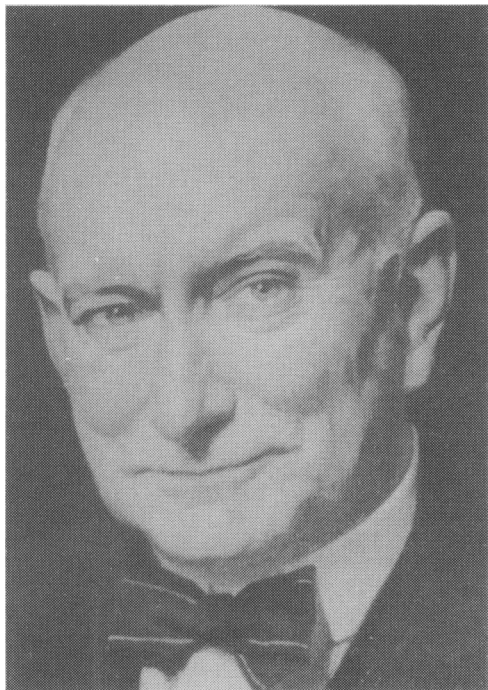


FIG. 1. *Professor Charles G. Lowry*

### RAISING THE FUNDS

To find the money — estimated at £100,000 — a special public meeting was held in the City Hall, Belfast, on 16th May 1928 to launch the scheme. Professor Lowry (Fig. 1) was fortunate in that he had been able to interest the then Duchess of Abercorn, wife of the first Governor of Northern Ireland, in the project. At the meeting Her Grace moved the motion that “the necessary funds be raised to build and equip a new maternity home with 100 beds adjoining the Royal Victoria Hospital”. The main speaker, however, was Professor Lowry and a report of his address “Ulster’s New Maternity Hospital” was produced. A great deal of his speech consisted of material taken from his memorandum (Fig. 2) and again the reason he most stressed was the maternal mortality statistics which he reiterated. These were, as previously quoted, a maternal mortality of 6 per 1,000, 150 mothers died per annum, three per week, one every

second day. Professor Lowry ended his speech in the City Hall quoting these lines which John Masefield had dedicated to the memory of his mother —

“What have I done to keep in mind  
My debt to her and womankind?  
What woman’s happier life repays  
Her for those months of wretched days.  
.....  
What have I done, or tried or said  
In thanks, to that dear woman, dead?”

The menfolk of Northern Ireland responded to this appeal with such generous donations that the Board of Governors were able to announce at the opening ceremony of the new hospital costing approximately £130,000, that it had been opened free from debt.

### BUILDING THE HOSPITAL

The Royal Maternity Hospital was to be built as a separate unit beside the Royal Victoria Hospital, with its own administration but working in conjunction with the

older hospital. To complete the proposed and agreed amalgamation, a "Bill" had to be passed in Parliament which, after coming before a joint committee of the Northern Ireland Parliament, passed unopposed with its third reading on 29th April 1931. The architects for the new hospital were Messrs Young & McKenzie and the builders McLaughlin & Harvey.

### THE OPENING DAY

The great day finally arrived when the hospital in Townsend Street ended its career and closed its doors on 1st August 1933. The Matron, her nursing staff, ten mothers and six babies moved into the new Royal Maternity Hospital. Here, in the new hospital was pride and assurance of youth, pride in no vain glorious sense, but pride in its parentage and in the traditions which its predecessors had handed over to it and which it would endeavour to emulate— even surpass.

According to the first Annual Report, the last baby born in Townsend Street was David Hay— on 28.7.83. His mother was Helen Hay, as recorded. However, the name Annie Shields who had a daughter the same day, appears on the next line, so I wonder if the Report is correct? As no time is recorded we cannot be certain. The first baby born in the new hospital was Francis Wisdom (6 lb 4 oz), born at 9.45 a.m. on 1st August 1933. His mother was Mrs Mary Alice Wisdom.

When opened, the hospital had 100 beds as planned, but as the Building Committee had to leave the construction of the Nurses' Home until further funds were available, 40 beds out of the 100 were allocated to nursing and domestic staff. This state of affairs was not to be remedied until the New Nurses' Home opened its doors in 1937. This later became Musson House, named after Miss Musson who was Matron of the Royal Victoria Hospital.

### THE OFFICIAL OPENING DAY

On Saturday, 21st October 1933, Professor Lowry's great ambition was officially realised. Belfast's splendid new maternity hospital, designated by His Majesty King

## Ulster's New Maternity Hospital.

Patroness : Her Grace The Duchess of Abercorn.

*Some Reasons why all Ulster People and all Friends of Ulster should give their generous HELP TO BRING INTO BEING the projected Maternity Department of the Royal Victoria Hospital.*

A reprint of the ADDRESS given  
by Professor CHARLES G. LOWRY, M.D., F.R.C.S.,  
at the City Hall, Belfast, on 16th May, 1928.

The work of the Belfast Maternity Hospital was started in 1793, in a small way, by a few ladies, under the name of "THE HUMANE FEMALE SOCIETY." In 1825 a new building was erected in Clifton Street, and the present Hospital in Townsend Street was opened in 1904.

"Children bring a great deal of happiness and joy into our lives."

—Marquess of Duferin and Ava.

"We have deplorably insufficient provision in Belfast for that very important department of medical science, maternity accommodation."

—Prof. J. A. Lindsay, F.R.C.P.

"I can imagine no better Memorial to a Mother than a good Maternity Hospital."—Prof. C. G. Lowry, F.R.C.S.

C. G. G. BAIRD, LIMITED, BELFAST 5771-5-28

### FIG. 2.

*Photograph of front page of Professor Lowry's address on 16th May 1928.*

George V “The Royal Maternity Hospital”, was officially declared open by Mrs Stanley Baldwin OBE who came to Belfast for this purpose on the invitation of Her Grace, the Duchess of Abercorn, who had done so much to further the scheme of providing Belfast with a maternity hospital of which it could be proud.

The opening ceremony was a grand affair, being reported in all the newspapers with different accounts and photographs. The ceremony was broadcast by the BBC. After the opening there was the usual conducted tour of the hospital. The Duchess of Abercorn and Mrs Baldwin inspected, apart from other areas, the Rosalind Nursery which was named after the Duchess. A personal comment, made subsequently by C.H.G. Macafee, noted that the man who was the driving force behind the scheme was not on the platform but in a seat at the back of the marquee. Of course, he meant Professor Charles Gibson Lowry.

About the same time, the following words were expressed by Dr C.S. Thomson, the then Medical Superintendent Officer of Health for Belfast: ‘The Belfast Maternity Hospital was established in the reign of King George III and an institution which has lived through all the storms and stresses since — the buffetings of fate, the overthrow of kingdoms and the crashing of thrones — must be one blessed by Divine Providence and respected of mankind’. Perhaps these sentiments could be repeated today.

The first and only baby born on the official opening day was a daughter to Mary Jordan. Baby Jordan is now Mrs Morrow who will be 50 years old tomorrow.

#### SOME EVENTS OVER THE FIFTY YEARS

During the preparation of this Address it soon became obvious that it would be quite impossible to mention everything which had occurred in the hospital over the past 50 years. I have therefore chosen important events which I hope will not only be of interest but were also milestones in the hospital’s history.

##### *The Matrons*

By long tradition, the Matron was “the boss”. She could be compared to the Captain of a great liner, in charge of all the crew and responsible for the passengers. Although time has changed her role, in the Royal Maternity we still like to think of our District Nursing Officer as “Matron” with all the status that went with her in the past. We have had seven Matrons over the 50 years.

1933—34	Miss Waddell
1934—37	Miss Clark-Kennedy
1937—52	Miss Sparkes
1952—61	Miss Margaret Brooksbank
1961—73	Miss R.C. Perkes
1974—80	Miss Annie Mann
1980—	Miss Elizabeth Duffin

Miss Waddell was the Matron in Townsend Street and orchestrated the change-over. For reasons not recorded, she resigned on 1st September 1934 — less than one year after the official opening.

On 16th November 1934, Miss Clark-Kennedy, Matron of the Maternity Wing of the Radcliffe Infirmary, Oxford, was appointed at a salary of £216 — £30 more than



the advertised salary — so she must have been something special. Three years later she resigned and was soon replaced by Miss Sparkes who had been a Sister in the Midwifery Department of the Middlesex Hospital. I am sure some of you will remember her. I understand the name was appropriate. In 1952, she resigned, after 15 years' service and Miss Brooksbank was appointed. During her reign she was associated with the new unit for the preparation and sterilisation of infant feeds. She was also associated with a central linen supply within the hospital, a further redesigning of the nurseries for the care of sick and premature infants, and the acquisition of the "Perspex" cots. The prototype of the stand was designed in Birmingham and the "Perspex" crib in Belfast. The money was donated by Mrs Byers, wife of the Chairman, in the name of their three sons. The Chairman, of course, was the son of Professor Byers who, as stated earlier, was the Professor of Obstetrics before Professor Lowry.

Miss Brooksbank's successor, Miss Rosemary Perkes came to Belfast from the General Lying-in Hospital, London. She transferred the sewing and linen services, and kitchen and meal services, to lay administration. She closed down the District Midwives' Home in North Queen Street and centralised these services from the hospital. She introduced mothercraft and physiotherapy classes, commenced the training and introduction of nursing auxiliaries, and ward clerks — all changes that today are just part of the scene. If one cares to summarise her many achievements it probably would be that she relieved the midwife of many duties and in so doing allowed her more time to practice her profession.

Miss Perkes left in 1973, the year of the integration of the Health and Social Services and the implementation of the recommendations of the "Salmon Report" in Senior Nursing Staff Administration Structure. The result, for good or evil, was that the name "Matron" was replaced by that of "Principal Nursing Officer". Thus, when her successor Miss Annie Mann, commenced duties in January 1974 we had a new type of nursing administration which not only included the hospital but also the community. For a while it all seemed to be the numbers game, the various grades of administration being known by number, and this continued down the chain of command to the Sister. I can still hear our well known Senior Sister in labour ward uttering some unrepeatable remarks about being a No. 7 or 8 when, of course, she was No. 1 in labour ward and would always be No. 1.

By now, five years of the "troubles" had affected the hospital. Recruitment of students and retention of trained staff was down. In fact, we had to reduce the beds to 73 for a time. A recruitment campaign by Miss Mann and Miss Robb, District Nursing Officer of the Royal Victoria Hospital, gradually and successfully increased the numbers again until further required increases were limited due to financial difficulties. Unfortunately, today's staff is below that required, due to the financial stringencies, but one can only hope our political masters will not tighten the strings to such an extent that the highest standards of care are affected. With the responsibilities of the community services, Miss Mann was upgraded to Divisional Nursing Officer. She retired in 1980 and was succeeded by the present DNO, Miss Elizabeth Duffin.

### *The Training of Midwives*

The evolution of the handywoman of the early 19th century to the highly professional and skilled midwife of today, holding first her general nursing qualifications,

followed by 18 months training in midwifery, is interesting, and is shown in Table I which records the changes over the years. Note that 50 years ago and for many years after, the Matron was head of the training school, whereas today there is a Northern Ireland College of Midwifery under its excellent Director, Miss Uprichard. This College embraces the training schools in Jubilee Maternity, the Ulster Hospital and Altnagelvin Hospital, Londonderry.

TABLE I  
*Requirements and training of midwives*

<i>Year</i>	<i>Head of School</i>	<i>Registration</i>	<i>Requirements</i>
1916	Matron	Central Midwives Board (Ireland)	3 months — anyone
1916-1922	„	„	4 months — SRN
1922-1926	„	Joint Nursing/ Midwives Council	6 months — untrained
1926-1938 (12 years)	„	„	6 months — SRN 12 months — untrained
1938-1969 (32 years)	„	„	12 months — SRN Part I — 6 months „ II — 6 months
1970	„	„	12 months — SRN
1971	„	NI Council for Nurses and Midwives	12 months — SRN
1974	Central School of Midwifery (PAEO)	„	12 months — SRN
1980-June 1983	„	„	18 months — SRN
July 1983-date	NI College of Midwifery (Director)	National Board for Nurses, Midwives, and Health Visitors	18 months — SRN

#### *Undergraduates*

The number of undergraduates trained over the past 50 years has increased. In 1933, when the hospital was opened, 45 medical students trained. Twenty-five years later, in 1958, accommodation for 10 students was available and a two-month residency programme was mandatory. Thus, approximately 60 students were trained annually in the Royal Maternity. Rules were stricter in those days. Full attendance at all classes was expected. Students were summoned by a bell to the labour ward for the delivery of every baby — night or day. No students were allowed to leave the hospital without the permission of the senior tutor. The present accommodation takes 15 students at a time for a 10-week period. This increased period is associated

with the inclusion of gynaecology and a two-week period is spent in a hospital outside Belfast. Both innovations are appreciated by the students, including perhaps, also some relaxation of the rules.

### *Postgraduates*

As a postgraduate training school we take those who are sitting the MRCOG examination with the aim of specializing in obstetrics and gynaecology. There is also a DRCOG programme for those either specializing or taking part in the general practitioners' vocational training scheme for their own MRCGP examination. Post-graduates from many countries have trained in the Royal Maternity. As with our own postgraduates, they may rotate through the other three Belfast hospitals — Jubilee, Ulster and Mater — and one or other of those outside Belfast. There was a preponderance from Australia and Malaysia in the 1950's, Africa in the 1960's, and from then on a gradually increasing number from the Middle East.

Those taking the Membership examination of the Royal College of Obstetricians and Gynaecologists have brought distinction to the postgraduate school. In the past 25 years five of our postgraduates have taken the Gold Medal for first place in the examination; they are, D.R. Aicken (graduated in New Zealand 1965) and four Queensmen — J.S. Robinson (1974), H.R. Skelly (1975), R.S. Sungkur (1978) and J.H. Price (1982).

The traffic from overseas to Belfast has not all been one-way for many of our Registrars/Senior Registrars are encouraged to go abroad. The popular areas are Canada, Australia, Uganda, Zimbabwe and South Africa. Our record of those

TABLE II  
*Postgraduates of the Belfast School of Obstetrics who became Professors*

<i>Name</i>	<i>University qualified</i>	<i>University Chair</i>
CG Lowry	QUB	QUB
RJ Johnston	„	QUB
CHG Macafee	„	QUB
JHMck Pinkerton	„	Queen Charlotte's/Chelsea London
W Thompson	„	QUB
TM Roulston	„	Manitoba, Canada
CR Whitfield	„	Manchester/Glasgow
JS Robinson	„	Newcastle, NSW, Australia
DM Jenkins	„	University College, Cork
NA Beischer	Melbourne	Melbourne, Australia
DR Aicken	New Zealand	Otago, New Zealand
KK Bentsi-Enchill (deceased)	Ghana	Accra, Ghana
SH Tow	Singapore	Formerly Singapore
CStJ Harding	Dunelm	Morovia, Liberia
IM Brown	St Mary's, London	Harare, Zimbabwe
OA Ojo	Ibadan	Ibadan, Nigeria

postgraduates who trained in Belfast and subsequently got a "Chair" would be hard to beat. Table II shows 16 of them although there may be more. Nine were graduates of Queen's University of Belfast and, as you can see, over the hospital's 50 years all the Chairs in Obstetrics and Gynaecology at this University have been filled with distinction by Queensmen.

With few exceptions, all the consultants in Northern Ireland at the present time have spent some period of their postgraduate training in the Royal Maternity Hospital and the majority have held the senior tutor's post — considered the "top job" for the senior registrar. The senior tutor is responsible by tradition for the student and junior medical staff of all grades. The smooth running of the hospital depends largely on him as he acts as liaison between nursing, medical and administrative staff.

### *Changes in Maternal and Fetal Mortality*

One does not like to use too many statistics on an occasion such as this, but unfortunately these are essential to relate demand on our hospital accommodation, and obstetricians use the survival of mother and fetus to assess whether or not what they are doing, or have been doing, is of benefit to mother and baby. Thus, I impose on you the following data for the past 50 years, with apologies.

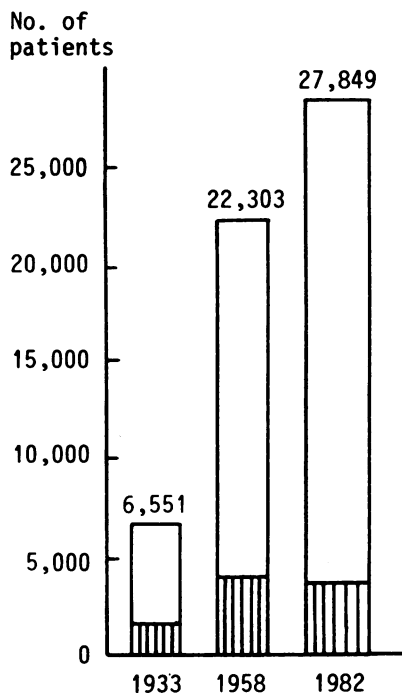


FIG. 3.

*Number of patients attending Royal Maternity Hospital antenatal department, 1933-1982. Hatched area shows new patients; remainder are reattendances.*

The increasing workload of the hospital's antenatal department can be seen in Figure 3. In 1933, 1,500 new patients attended; by 1958 the figure varying between 3,500 and 4,000; and remaining so to the present. The marked increase in reattendance figures is also seen and total attendances are now approaching 28,000, which is approximately 500 patients per five-day week, or 100 per day. The amount of work this generates could only be appreciated by actually attending one of the clinics.

From Table III it can be seen that approximately 133 thousand patients have been admitted and over 105 thousand babies born. The marked increase in the last 25 years is clearly seen. These figures are all the more striking when we look at Figure 4 showing the increasing number of admissions with very little increase in the number of beds. Is it any wonder our bed occupancy is over 100 per cent.

The fall in the hospital maternal mortality from approximately 27 per 1,000 in 1933 to none in the last five years up to December 1982, has been rewarding. In fact, it has been virtually under 1 per 1,000 for the past 25 years (Fig. 5).



TABLE III

*Total patients admitted and infants born in the Royal Maternity Hospital, 1933-1958*

	1933 └───┬───┘ (25 years)	1958 └───┬───┘ (25 years)	1982 Total
Patients admitted	52,514	80,653	133,167
Infants born	39,625	65,682	105,307

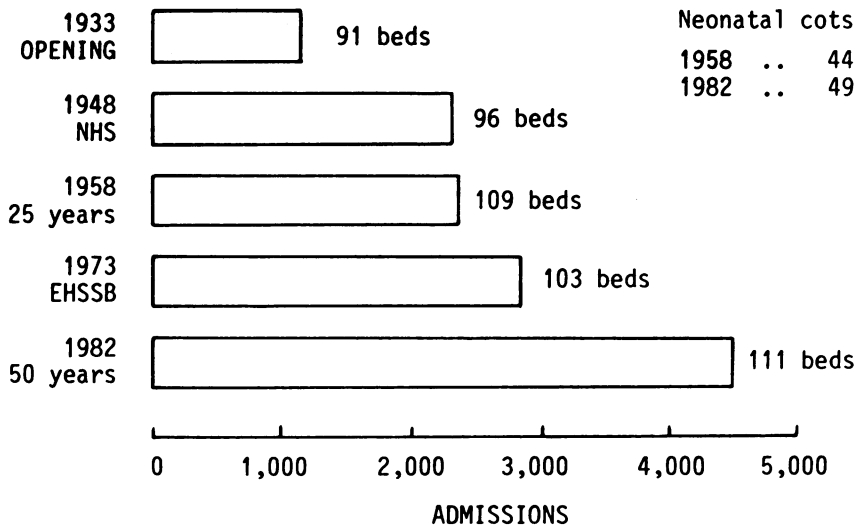


FIG. 4. *Number of admissions/beds at important dates in the 50-year history of the Royal Maternity Hospital*

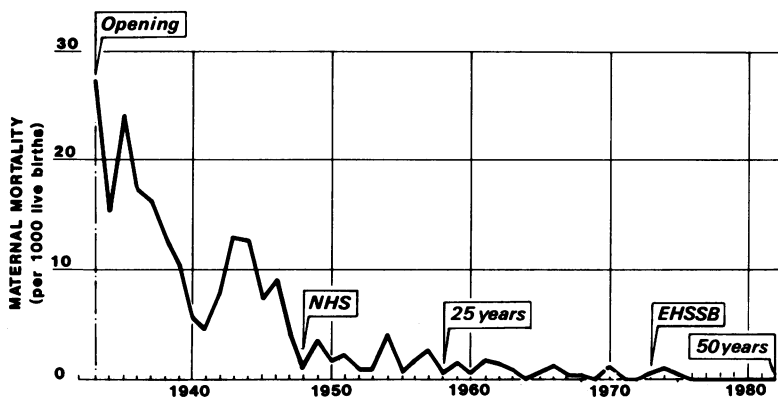


FIG. 5. *Maternal mortality, Royal Maternity Hospital, Belfast, from time of opening in 1933 to 1982*

Figure 6 shows the large increase in the number of babies born, from approximately 700 in 1933 to nearly 1,800 in 1958 and by 1982, nearing 3,600, that is, double since 1958, with about the same number of beds. The stillbirth rate has been reduced from 90 per 1,000 in 1933 to about 10 per 1,000 in 1982, and the neonatal death rate from 35 per 1,000 in 1948 to 10 per 1,000 in 1982.

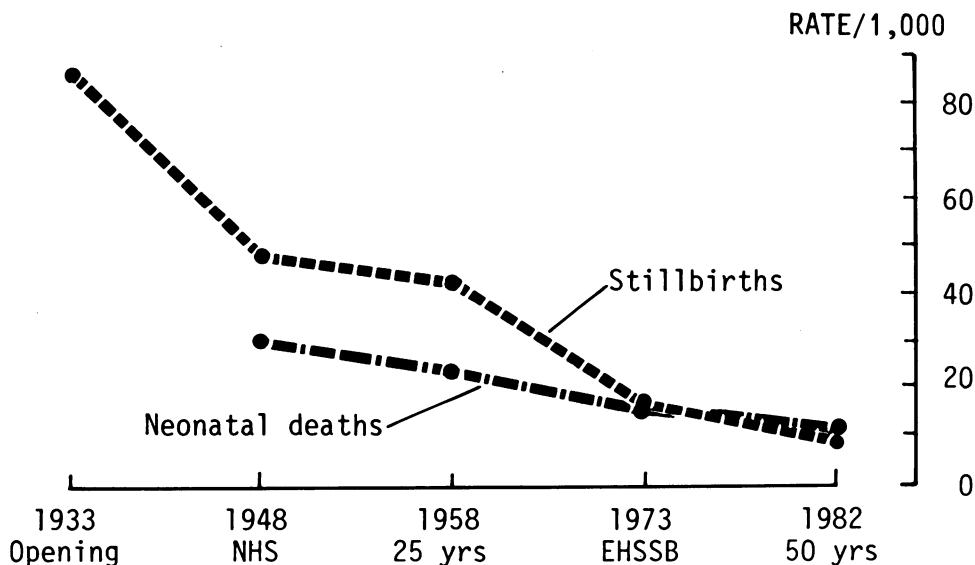


FIG. 6.

*Stillbirth and neonatal death rates, 1933-1982, at important dates in the 50-year history of the Royal Maternity Hospital, Belfast*

The improvement in the perinatal mortality (that is, stillbirths and neonatal deaths in the first week) for the past 12 years from over 40 per 1,000 12 years ago to less than 20 per 1,000 for the past 3 years — more than halved. I mention this because the fall in perinatal mortality for these years has been, for the most part, attributable to the advent of the neonatologists and the sophisticated equipment for intensive and special care of all babies requiring it, in particular those of low birth-weight. Their increased survival has been a major advance and a credit to all those who look after them.

To produce these very creditable results, many changes have occurred and only a few can be highlighted in any detail. However, this must not detract from the importance of the others such as the control of infection by sulphonamides and antibiotics which brought about the first dramatic fall in maternal mortality by eliminating that killer, puerperal sepsis. Such an important episode in medicine would deserve its own Presidential Address.

The discovery of blood groups and the formation of the Blood Transfusion Service allowed for the survival of many patients who would previously have died from that other great killer — postpartum haemorrhage.

### *Placenta Praevia*

These discoveries had a worldwide effect on maternal and fetal mortality, but there were others, the most famous of these being the conservative management of placenta praevia advocated by the late Professor C.H.G. Macafee (Fig. 7) — delivery could be postponed in the majority of cases until the fetus was mature enough to survive. The work was carried out in the Royal Maternity and the management he advocated was adopted throughout the world. It resulted in the saving of an incalculable number of mothers' and babies' lives, and was to assure the Belfast School of Obstetrics a place in medical history and establish its international reputation.

When the hospital opened its doors in 1933, the maternal mortality in the United Kingdom was about 5 per cent and the fetal mortality 50-60 per cent. The United Kingdom figures are given as the hospital figures were not recorded for placenta praevia, but it would have been about the same. Professor Macafee's policy, introduced in 1936, led to a marked reduction in the maternal and fetal mortality over the years. As can be seen in Table IV, the most recent figures are, no maternal death and a fetal mortality of under 5 per cent. Perhaps even more striking is that only three mothers have died from the condition since conservative management was introduced 47 years ago. Although, as Betsy Trotwood said to David Copperfield, "It's in vain to recall the past unless it works some influence on the present", this recognition of the influence of maturity on fetal survival in placenta praevia was undoubtedly a major contribution to obstetrics and perhaps one of the earliest examples of "perinatal medicine".

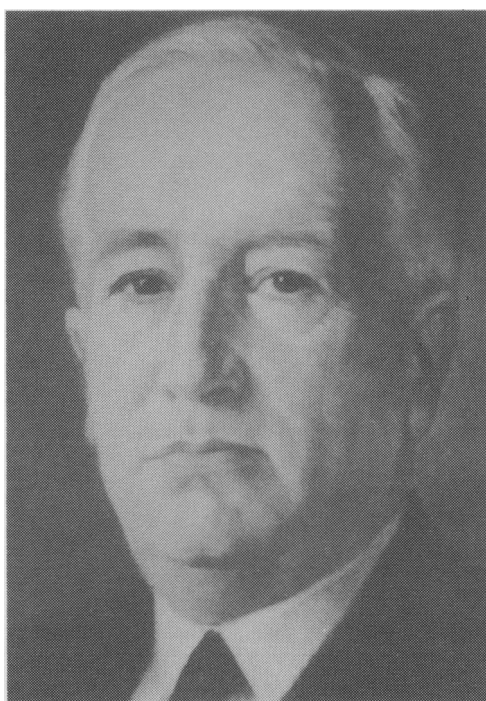


FIG. 7. *Professor C.H.G. Macafee*

TABLE IV  
*Maternal and fetal mortality in placenta praevia,  
Royal Maternity Hospital, Belfast, 1937-1982*

	<i>No. of cases</i>	<i>Maternal mortality</i>	<i>Fetal mortality</i>
1937-45	191	1 (0.52%)	42 (22.0%)
1946-53	200	0	24 (11.9%)
1954-58	130	2	16 (12.5%)
1978-82 (5 years)	312	0	22 (4.3%)

### *Rhesus incompatibility*

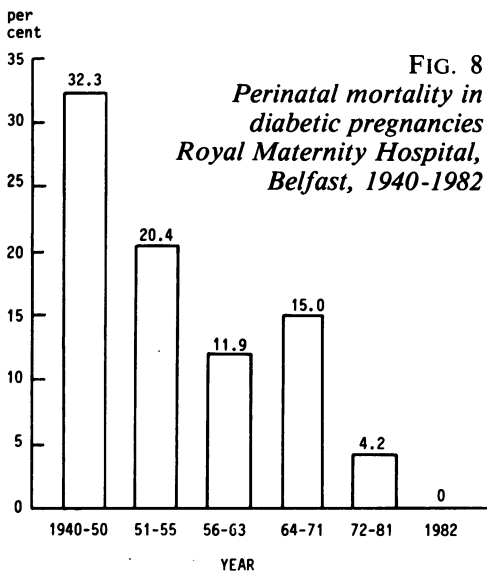
Another important advance was the discovery in 1940 by Landsteiner and Weiner of the Rhesus factor, and the report the following year by Levine that haemolytic disease of the newborn was due to Rhesus incompatibility between mother and fetus and could result in babies like this who had died from the disease. At this time the fetal mortality in the hospital from Rhesus incompatibility was over 75 per cent. Numerous advances in our knowledge and management of the condition have occurred over the years, each bringing an improvement in the number of babies surviving (Table V).

TABLE V

*Rhesus incompatibility, Royal Maternity Hospital, Belfast, 1948-1982*

<i>Date</i>	<i>Patients delivered</i>	<i>Affected (Rh antibodies)</i>	<i>Fetal loss</i>
1948	12	7	57%
1955	67	54	31%
1968	237	161	19%
1975	116	65	26%
1981	43	36	11%
1982	62	27	7%

The final breakthrough came in 1968-70 with the introduction of Rhesus prophylaxis. This simple procedure (comparable to any other vaccination procedure) to prevent antibody formation in the mother should virtually eliminate the condition and will rank as one of the greatest advances in obstetrics.



### *Pregnancies complicated by Diabetes*

The Royal Maternity Hospital in Belfast had one of the first metabolic/antenatal clinics in the United Kingdom. This is a combined clinic run by physicians and obstetricians and was started in the late 1950's by Professors Macafee and Montgomery, and has continued with Dr Hadden, myself and our senior registrars. This combined clinic allows closer supervision of the diabetic mother in pregnancy, and the dramatic fall in perinatal mortality is shown in Figure 8. The particularly low figure achieved in the 10 years 1972-81 is due mainly to the appreciation that the patient's blood sugar must be kept to as normal a level as possible. This has been



possible with the use of a Glucometer by patients. Fat babies dying before birth are now rare. In addition, the skill of the neonatologists has played an important part, which can be judged by the fact that no diabetic baby born alive has died in the past 10 years, unless it had an abnormality incompatible with life — an excellent record.

### *The Genetic Clinic*

Over the past 20 years, fetal malformations have been the primary cause of still-birth in the hospital and are now the second most important cause of neonatal deaths, being surpassed only by prematurity. The infant mortality has fallen from all causes since 1980 but remains the same for congenital abnormalities. The Department of Medical Genetics at Queen's University of Belfast highlighted this problem even more when their figures were published in 1979, showing the incidence of common major abnormalities in Northern Ireland. This work revealed the horrible fact that in this province during the years 1974-1977 approximately 25 per 1,000 infants born had a potentially lethal or handicapping abnormality, that is, one in 40.

The first genetic/obstetric clinic in the Royal Maternity began in November 1969, with the aim of trying to diagnose and reduce the number of fetal malformations. To this clinic are referred patients from all over the Province who are at risk, eg, elderly mothers and those with a family history of abnormalities or who have already had an abnormal baby. At the present time, 20-25 patients at risk are screened each month—about 250 per year—and this would be only a fraction of the actual number of mothers counselled. The number of abnormalities detected averages about 10 per annum at the present time. Of these, two or three would be chromosomal and five or six neural tube defects. The numbers do not in any way relate to the time and care taken with each patient, but the workload is increasing and will continue to do so until the problem is under control. Our efforts to tackle this problem in our community today must not be restricted by cutbacks of any kind. Apart from the distress caused to patients and their families and its effect on the morale of those who look after the patients, the subsequent cost to the community is enormous. This is one certain way where money spent on prevention now will definitely prove to be a saving in the long term.

### *Ultrasonics*

The contribution of ultrasonics to obstetrics has been of the greatest value and one which has proved itself to be of immense benefit to mother and fetus. Increasing knowledge leads to increased demands for the service with the inevitable increased workload. Ultrasonics first made its appearance in the Royal Maternity Hospital in May 1968. The number of ultrasonic scans performed remained fairly constant until 1974. Since then the number of scans carried out in the "Day Unit" of this hospital has risen from 2,067 in 1970 to 7,954 in 1982 — a threefold increase. The numbers will continue to increase as biophysical monitoring of the fetus becomes more and more sophisticated and probably more reliable than biochemical tests. These ultrasonic scans are carried out by obstetricians of all grades and, in addition, we have two general practitioners who have two sessions each per week, providing a valuable service for which we thank them.

I am sure many have noticed my omission of that commonest of obstetrical problems—pre-eclampsia and also eclampsia and accidental haemorrhage. Although

still with us, improved antenatal care and control of maternal blood pressure, together with improved methods of monitoring, have resulted in a maternal mortality of nil and a fetal loss under 5 per cent, so these conditions, happily, are no longer a major problem.

### *Anaesthesia*

As in any other hospital, the anaesthetist has an important part to play in the safe operative delivery of mother and baby. Our present consultant and senior registrar anaesthetists have done, and still do, provide an invaluable service, operating the modern anaesthetic machines. The development of epidural anaesthesia for the relief of pain in labour and, in some cases delivery, has benefitted many patients and the demand is increasing.

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Today the presence of the husband at a delivery is now the norm in the majority of cases, whereas 20 years ago he would probably have been elsewhere fortifying himself for the big event.

We are always prepared to consider the consumer, provided the demands do not interfere with necessary medical care. Various types of "birthing chairs" are being investigated at present but, so far, in spite of the media, there has been no suggestion of "pulleys from the roof" for delivery in the upright position, or tanks for under-water delivery, but who knows what the next decade will bring. Perhaps "wet suits" will replace theatre garb for obstetricians while midwives will wear "bikinis".

There is a small but increasing demand for home confinements again and this, I think, most obstetricians would resist. Domiciliary midwifery had its place in the past but its disappearance has been to the benefit of both mother and baby. This hospital was responsible for a larger number of confinements at home (72 per cent) than in hospital (28 per cent) when it first opened in 1933, but by its 25th anniversary the trend had been reversed (30 per cent home; 70 per cent hospital), and today there is a hospital confinement rate of 100 per cent except in some exceptional circumstances. This does not mean to say that community midwifery has disappeared. Group practices with all their facilities are sharing the antenatal care of more and more patients with the hospital and this is to be encouraged. Anything that will reduce the number of patients attending the hospital antenatal clinics would be of benefit to both hospital and patients and would, in my opinion, lead to even better antenatal care.

In conclusion, as tomorrow is the 50th anniversary of the Royal Maternity Hospital, perhaps I should take you back to that great occasion 25 years ago when we celebrated our Silver Jubilee. A Service of Thanksgiving and Rededication was held in St Anne's Cathedral on the Sunday. A cherry tree was planted to commemorate the occasion. All the sisters received solid silver spoons, as did the cook and others who had given long service. Also given a spoon was Mrs McCrystal who had the first and only baby on 21st October 1958. On the spoon is the hospital crest designed by Miss Praeger and commissioned by Mrs Maitland Beath in memory of her father and mother, Mr and Mrs R.M. Young and Christine Grace her daughter (Fig. 9).

Since the Silver Jubilee, the upgrading of several areas has taken place and two major structures have been added — the new extension and the new labour suite.

The new extension opened in June 1965 provided new beds, residential and office accommodation. Note carefully, I did not say additional beds for, as previously seen, the number of beds in 1933 planned for 100 and originally 50, had by the 25th anniversary increased to 109. At present the number of beds is officially only 111. The show-piece is the new labour suite which opened in 1971 and provided the hospital with one of the largest and most up-to-date and well-equipped labour suites in Europe.

Everyone involved in the hospital believes like our predecessors. Only the best is good enough for the pregnant woman and to provide this we will strive to improve the care we gave in the past for the patients and their babies. We will continue undergraduate and postgraduate training programmes of doctors and midwives.

Beckett said, "There is nothing that solidifies and strengthens a nation like making the nation's history, until the history is recorded in books, or embodied in customs, institutions and leaders". How well these words might apply to the Royal Maternity. The present hospital still remains proud of its amalgamation with the Royal Victoria Hospital started 50 years ago, and I would hope our colleagues there with whom we share the site and have the closest liaison, will concede that the Royal Maternity Hospital, situated in the middle of The Royal complex, is one, if not the largest, jewel in the Royal crown.

In thanking you for listening so patiently, let me finally say this to you. In troubled times we live again, but fear not, for those who have gone before survived the same, and through it all, they made, a hospital of widespread fame. Therefore, let us go forward in confidence, knowing that if we can but emulate their achievements, the greatness of the Royal Maternity Hospital shall remain.

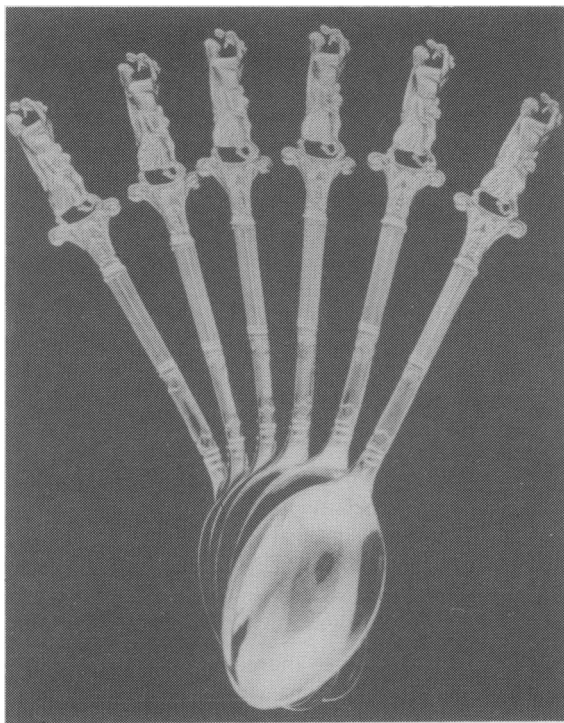


FIG. 9  
*Solid silver spoons presented on the occasion  
of the silver anniversary of the  
Royal Maternity Hospital, Belfast.*

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I am most grateful to all the medical, nursing and administrative staff who provided me with the material for this address, particularly Miss D. McAuley, Hospital Secretary, and Miss B. Ross, Records Officer. My thanks also to those two, without whose help no address of mine would ever be produced, Mr Ronald Wood for the photography and my secretary Miss May Weller. Finally, my sincere thanks to my wife and family who had to tolerate me during the preparation of this address.

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# **A HOSPITAL FOR ALL SEASONS**

by

**J. A. WEAVER, MD, FRCP, DL**

**Annual Oration at the opening of the 1983-84 Teaching Session,  
Royal Victoria Hospital, Belfast.**

I WISH to thank the Medical Staff for the honour of giving the Opening Address. I wish to acknowledge my indebtedness to the inherent traditions of this hospital as shown by my former teachers, my colleagues and the nursing profession.

Only related to a degree to what I hope to say is a prayer of Christina Rossetti: "O Lord, move us by Thine example to show kindness and do good. Grant us such patience and forbearance with all sufferers that in our stumbling walk and scant measure, they may yet discern a vestige of Thee, and give Thee the glory".

The address to the new students of the hospital — hallowed though it may be by long tradition — is founded on the mistaken principle that old men have something useful to say to young men, and the concept is further flawed in that young men will not listen. And so it should be. As Benjamin Jowett said, 'I hope our young men will not grow into such dodgers as (we) old men are'.

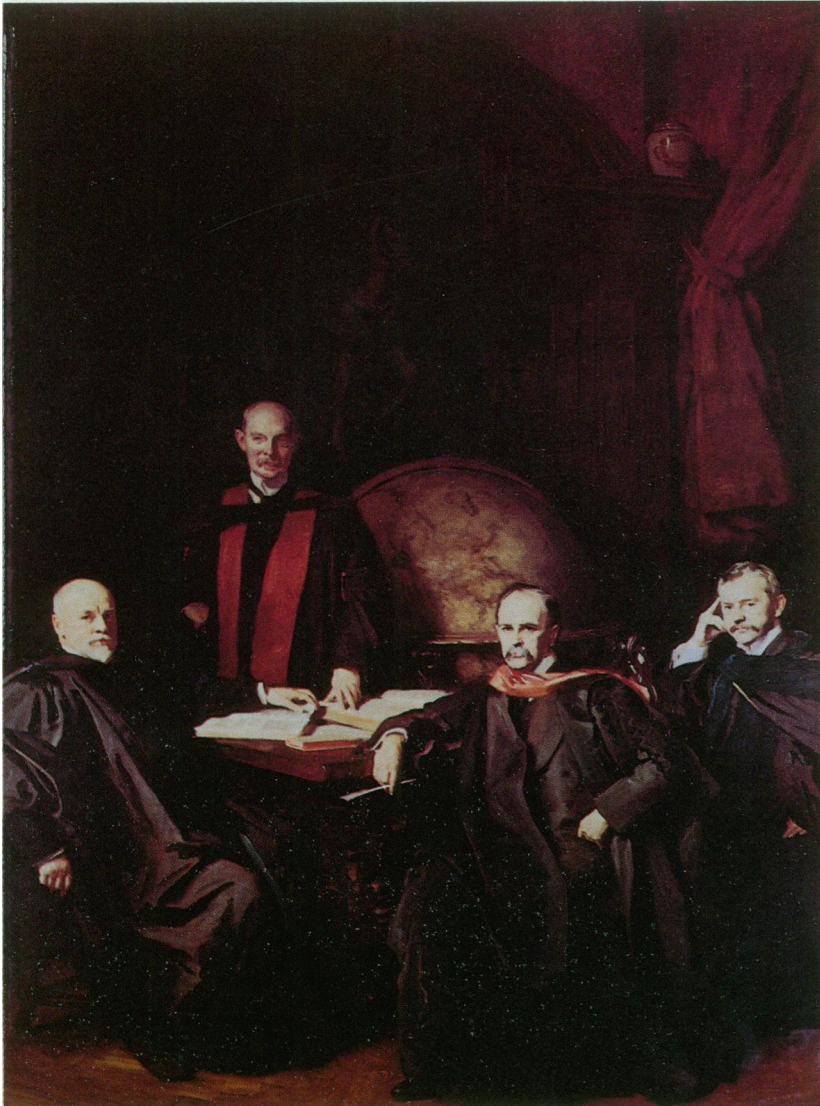
"A man for all seasons" — Sir Thomas More, so described by Robert Whittington in 1520. "More is a man of an angel's wit and singular learning. And as time requireth a man of marvellous mirth and pastimes and sometimes of a sad gravity. A man for all seasons". Since David Bolt's play, these words have become somewhat hackneyed and over-plagiarized and I do offer a scant apology in their use again today. I am also reminded of the last message Henry VIII sent to Sir Thomas More, "The King's pleasure is further that at your execution you shall not use many words". On today's scaffold I will attempt to heed that advice.

Having made this reference to Sir Thomas More, I confess that most of what I propose to say has nothing to do with him and at this point he could almost take his exit. However, I admire his portrait and one cannot use the phrase "for all seasons" without acknowledging him. My early thoughts had been to attempt to define 'a doctor for all seasons' but reflection prompted me that this would not be an easy task and that such an ideal doctor, if fully characterized, might turn out to be an embarrassingly rare species. Mr Chairman, I have no difficulty in defining my surgeon for all seasons and I simply emphasize the universal pleasure your appointment to the Order of the British Empire has given\*.

If not "a doctor for all seasons" then let me admire "a hospital for all seasons". The choice of this wider horizon reflects Theodore Fox's phrase "the greater medical profession". In 1956 he wrote, "Should we perhaps revise our ideas and regard everybody who does medical work as belonging to what one might call the greater medical profession?" Certainly this concept of Fox easily includes the nursing

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(\*Chairman of Royal Victoria Hospital Staff — Willoughby Wilson FRCS — appointed OBE 1983)



*The original Johns Hopkins Medical Faculty  
painted by Sargent in 1905.*

(Reproduced by kind permission of Robert M. Heyssel MD,  
Executive Vice President and Director of The Johns Hopkins Hospital,  
Baltimore, Maryland, USA.)

profession, physiotherapists, radiographers, electrocardiographers, social workers, pharmacists, laboratory workers and clinical secretaries. Perhaps after that the frontiers of the “greater medical profession” get more difficult to define. I will not attempt to delineate it entirely but I am happy to include everyone who comes to this place — to this hospital — each morning with the idea that the day’s work, that the day’s task, that the day’s commitment is about caring for the sick.

To any sceptic in the audience who asks, “Can I say that and not recall the industrial action of last year?”, I would reply that most of those involved were and are underpaid and also that many members of the greater medical profession, as I have just outlined it, carried on at work with exemplary devotion during that time. Not only are they underpaid in absolute terms but sadly also in relative terms in the value that society puts on those who work for it.

A hospital for all seasons. I have had the pleasure and privilege of working in two such hospitals. The first of these hospitals began in this manner. On Christmas Eve 1873, in the city of Baltimore, Maryland, a wealthy bachelor died. (I make no comment on the fact that he was both a bachelor and wealthy!) That merchant — by name Johns Hopkins — left his fortune of seven million dollars for the establishment of a university and a hospital. It is believed he felt “A university, for there will always be youth, and a hospital for there will always be suffering”. The illustration reproduces the painting of the original Medical Faculty of the Johns Hopkins Hospital — William Welch, Professor of Pathology; William Stewart Halsted, Surgery; William Osler, Medicine; Howard Kelly, Obstetrics.

John Singer Sargent painted this portrait in 1905. Sargent, an American born in Florence and educated in Paris, became the foremost portrait painter of his time. He was commissioned to paint the first four heads of department at Johns Hopkins and persuaded them to meet in London to pose for him. There must have been a philosophic vein to Sargent for he once said, “Every time I paint a portrait I lose a friend”. Sargent painted Welch’s head in one sitting, but took much longer with the others. Osler’s head was completely painted out and re-done. A widely quoted legend maintains that because of a disagreement with Halsted, Sargent painted him in pigments that would fade.

For many reasons, it is William Osler that I wish to describe particularly, but a brief sketch of the other three is difficult to resist.

William Welch, Professor of Pathology, discoverer of *Clostridium Welchii*, Dean of the Hopkins Faculty for 40 years, and during that time the most influential pathologist in the United States, and administrator of the Rockefeller Foundation. Otherwise, a bachelor, incessant cigar smoker, overweight — often eating five or six dessert helpings. His gout he described as ‘absurd and unmerited’. Of interest, Welch was descended from a Philip Welch who, in 1654, was kidnapped from Ireland at age 11 by Cromwell’s soldiers and sold in Boston harbour as an indentured servant. (There are several other Irish connections in today’s story and I will acknowledge them as they occur.)

Halsted, Professor of Surgery. Early medical experiments with cocaine led to life-long drug addiction. Before Halsted’s day, surgery everywhere was a bloody ordeal based largely on speed and brevity of operation. To such traumatic practices,

Halsted's approach was the exact opposite. He laid the greatest stress on the gentle handling of tissue, on the complete control of haemorrhage, and on the accurate reapproximation of divided tissues. Time passed unnoticed as he studied the best possible approach to the problem in hand. There is a famous statement by Charles Mayo after visiting Halsted's clinic that, "He had never before seen the upper part of an incision heal before the lower part was closed". In his personal life Halsted was just as perfectionist. Though living in Baltimore, his shoes and clothes were custom-made in London from leather and cloth especially chosen by him. When entertaining, he personally went to the market to select the food and supervised the laying of the tablecloth which was ironed after being accurately placed on the table. Halsted, writing about his future wife, 'In the winter of 1889 the nurse in charge of my operating room complained that the solutions of mercuric chloride produced a dermatitis of her hands. As she was an unusually efficient woman I gave the matter my consideration and one day in New York requested the Good Year Rubber Company to make as an experiment two pairs of thin rubber gloves with gauntlets''. (And that was the beginning of the use of rubber gloves in surgical theatres.)

Kelly, the obstetrician, was descended from a family from Portadown. He had fundamental religious convictions often gathering the operating room staff together before an operation to say a prayer. (The Chairman remarked to me that he thinks this would be a good idea and is perhaps needed in some of the surgical wards, but he thinks it might be dispensed with in Wards 19/20.) It is said of Kelly, "If he had never written a line and never performed an operation he would still be classed as one of the great men of his day for the men he trained". (That description would fit another great obstetrician — Charles Horner Greer Macafee.)

However, Osler is my "doctor for all seasons". His biography written by the great neurosurgeon Harvey Cushing, opens, "William Osler the youngest son in a family of nine was born July 12th 1849 in a parsonage at Bond Head, Tecumseh County near the edge of the wilderness in what was Upper Canada. How this came about as to place, time and circumstances needs telling from the very beginning". Because his birthday was July 12th, William was his Christian name on the insistence of local orangemen, members of his father's parish. Osler's childhood was one of some physical hardship because of the primitive nature of that area of Canada at that time. Osler, throughout his life, harked back to many of these early influences. The Reverend Johnson, an ardent naturalist, taught him the use of the microscope, love of the Bible and Shakespeare. One criticism of Osler in later life was that he quoted too much from these sources. I am going to plead guilty today of quoting from other sources too frequently but I am comforted by Anatole France, "When a thing has been said and well said, have no scruple, take it and copy it." The danger for myself in not quoting others is to preach a personal viewpoint and very little discernment would distinguish the gap between the spoken word and the performance thereof.

Osler's undergraduate and postgraduate medical career was at McGill and Montreal General Hospital where, although practising clinical medicine, he did all his own post-mortems. As Osler said, "Pathology is the basis for all true instruction in clinical medicine". (It is appropriate to remember that Sir John Biggart, inspiration source of this lecture hall, an Oslerian by his own confession, would nod his head in agreement to that.) In 1884, at the age of 35, Osler became Professor of Medicine in the University of Pennsylvania, then regarded as the highest post in



medicine in the United States. After five years (1889) he was offered the new Chair of Medicine at the Johns Hopkins.

As a practising clinician, Osler was a therapeutic nihilist. He often quoted Oliver Wendell Holmes that if the entire pharmacopoea were dumped into the ocean it would be good for the patients but very bad for the fishes. Osler's international fame grew from his textbook 'Principles and Practice of Medicine' which, in his lifetime, was to run to eight editions and become a standard medical textbook, not only in English reading countries but in France, Germany and Spain. Osler started writing the textbook shortly after going to Baltimore and it is interesting that he used someone else's room. "He asked me if I would loan him the use of my room for an hour or so in the mornings. I, of course, said 'Yes' with great pleasure. The first morning he appeared with one book under his arm, accompanied by his secretary. When the morning's work was over he left the book on my library desk wide open with a mark in it. The next morning he brought two books with him, and so on for the next two weeks, so that the table, all the chairs, the sofa, the piano and even the floor, were covered with open books. As a consequence I was never able to use the room for a full six months". The success of the textbook depended on Osler's scepticism about the over-use of drugs. He introduced the new scientific approach to medicine based on pathology and the new sciences such as bacteriology.

About this time (1892) John D. Rockefeller had accumulated 'an unwieldy store of wealth' from the Standard Oil Company and the money was still coming in at a bewildering pace. He engaged a Baptist Minister, Frederick Gates, to help him. "I am in trouble Mr Gates. The pressure of these appeals for gifts has become too great for endurance". In 1897, the Reverend Gates, then in the employment of John D. Rockefeller, went on vacation taking with him a borrowed copy of Osler's 'Principles and Practice of Medicine'. The Reverend Gates was fascinated by the style of the book and realized how neglected previously had been the scientific study of medicine. Out of this assessment grew the Rockefeller Foundation involvement in support of medicine.

In 1905, after approximately 15 years as Professor of Medicine at The Johns Hopkins, Osler accepted a call to the Regius Professorship of Medicine in Oxford and, up to his death in December 1919, he achieved much for medicine in these islands, among which was the founding of the Association of Physicians with only two basic rules — "Its object shall be the advancement of internal medicine; the meetings shall be conducted in a manner that promotes friendship among physicians". Perhaps as I wished to end the Osler story at the point when he left Johns Hopkins, I should quote from his farewell address to the Canadian and American Medical profession. "I have three personal ideals. One to do the day's work well and not to bother about tomorrow. It has been argued that this is not a satisfactory ideal. It is . . . The second has been to act the Golden Rule, as far as in me lay, towards my professional brethren and towards the patients committed to my care. And the third has been to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with the courage befitting a man. I have made mistakes but they have been mistakes of the head, not

of the heart''. Dr Brew Atkinson recounts to me his first teaching in the Royal Victoria Hospital as an undergraduate. Dr Louis Hurwitz was lecturing to a small group of new students on the examination of the central nervous system and, relatively out of the blue said, "Write this down and remember it. Osler said medicine was neither an art nor a science but a way of life".

I have abbreviated too much and omitted Osler's marriage to Grace Revere, a descendant of Paul Revere the patriot of the American Revolution. The only son of the Osler's, Revere Osler, was killed in the Ypres salient in 1917. And much as I hope to show some thread running through my story today, I must record Major Harvey Cushing standing in a Flanders field watching the great grandson of Paul Revere, wrapped in a Union Jack, being lowered into the soggy ground. Mrs Osler — or rather Lady Osler — is not clearly defined in terms of her personality in Cushing's life of Osler. I rather fear, like most doctors' wives, she was on occasion taken for granted. Cushing was something of a martinet and autocrat and perhaps lacked insight into the feminine mind. There is a view that Cushing's characteristics as a martinet have been passed down successively to subsequent generations of neurosurgeons. A preview critic of this address suggested that I should not limit the Cushing inheritance to neurosurgeons and all doctors had their share of it. However, Lady Osler is on record as saying, "It was all very well for William to preach equanimity but have noted every time we had to move (and this was frequently) he had always a good excuse for not being there, leaving me if possible to cultivate equanimity in the uncomfortable circumstances."

The eventual significance of the Johns Hopkins Medical School stems in part from the Flexner Report. Abraham Flexner, the sixth of seven sons of an immigrant Hebrew couple from Western Europe, became the leading educational authority in the United States. His report entitled 'Medical Education in United States and Canada' appeared in 1910. The Report criticised most of the 155 medical schools for their poor standards. In fact, his report was so scathing that eventually only 76 of the 155 medical schools survived. Flexner found "a degree of merit" at Yale and "hopeful signs" at Michigan, but Johns Hopkins was his "shining model".

At this point some of the audience may be forgiven if they should think along the lines of Neville Chamberlain in 1938 who referred to the German invasion of the Sudetenland as "a quarrel in a far away country between people of whom we know nothing". Osler and the Johns Hopkins. A faraway people of whom we know nothing or maybe want to know nothing. I think not. I hope not. Mainly because Osler, it was, who re-defined medicine as an ancient and learned profession. The Hopkins because it led to a reformation of American medical education, eventually allowing American medicine to emerge as pre-eminent in medical research. To that end many of us owe allegiance and it seems to me a duty to acknowledge our respect for it and our thanks to it.

As regards our own hospital and medical school, William Welch was eventually succeeded by W. G. MacCallum and by Arnold Rich who trained John Henry Biggart at the Johns Hopkins. My immediate colleagues in endocrinology, David Hadden, Ken Nelson at the Ulster, trained at the Hopkins. The excellent virology institution on this site was, and is in part, Hopkins trained in George Dick and John Connolly. Also, Dermot Byrnes trained in neurosurgery and Dennis Biggart in pathology.

Less chauvinistic than that is this hospital's general indebtedness to American medicine:

John Logan, John Dundee, Gerry Black: Philadelphia.  
Frank Pantridge: Ann Arbor,  
Richard Womersley: Yale.  
Derek Gordon, Gary Love, Alan Kerr, Peter Walby, John Bridges,  
Sidney Lowry, Hilary Johnston, Ken Irvine: Boston.  
Terence Fulton: Cincinnati.  
John Geddes: Salt Lake City.  
Keith Buchanan, Aires Barros D'Sa: Seattle.  
Sam Webb: West Virginia.  
Jack Cleland, Hugh O'Kane, Joe Kennedy, Colin Russell: Mayo Clinic.  
Gordon Smyth: Memphis.  
Roy Gibson: St Louis.  
Desmond Archer: Chicago.  
Denis Coppel: Dallas.  
Sean Young: San Diego.  
Ian Carson: San Francisco.  
Ned Kennedy: Gainesville.  
Denis McDevit, Jimmy Riddell, Brew Atkinson: Nashville.  
Denis Johnston, John Hood: Denver.  
Julian Johnston: San Antonio.  
Morrell Lyons: Houston.  
Robin Shanks: Augusta.  
Alan Leonard: Buffalo.

And because Osler was born in Canada —

Tom Fannin, John Templeton, Conor Mulholland, Ian Adair,  
Joe McClelland, Sam Kielty and Ian Orr all trained in Canada.

Let me consider this hospital — the Royal Victoria — as my second hospital for all seasons. The Royal Victoria Hospital transferred to this site exactly 80 years ago, and on 27th September 1903, the patients were moved from the old hospital in Frederick Street. The staff, as Dr Robert Marshall recorded — 4 housemen, 1 lady superintendent and 2 assistant superintendents, 8 sisters, 4 staff nurses, 11 night nurses and 47 probationers. Something called the Telford Report appears to believe that this hospital could still be run by 4 staff nurses and 47 probationers!

Four score years on this site. The best of times and the worst of times. However, I do not share the view that the last 14 years have been the worst of times as far as this hospital is concerned. I have memories of this hospital that go back over 37 years and there are several in the audience whose memories extend back 60 years. 1946 is my first memory. A rattling, crowded, penny tram ride from the Ritz (ABC Cinema) corner up a busy, prosperous Grosvenor Road, full of bustling small shops. A gate-lodge with Victorian-clothed porters. Perhaps a dozen cars on the entire site. A busy outpatient hall where the main kitchen now is — then a general aroma of ether and disinfectants. The whole atmosphere sedate, assured, affluent, content, Royal. And now, an old and ageing building, surrounded by tracts of urban wilderness with graffiti on the hospital walls; and yet if you care to take a midnight walk down the

main hospital corridor, nothing has changed. The same suffering, the same uncompromising effort to meet it by young doctors and nurses. During the last 14 years the new challenge of the victims of senseless terrorism has been coped with on the surgical side and, more mundanely, the care of an increasing aged population on the medical side. Battle-scarred these buildings may be, but the scars only testify to the spirit of endurance of this hospital. "The Royal" is sometimes portrayed by the local media as being beset by many problems and unfortunate in its geographic location. I would not wish a hospital to be anywhere other than where it is most needed and that is where the Royal Victoria Hospital is. The challenge is here. The next terrorist victim is often within a short distance of here. The most deprived and frail elderly live within the shadow of this place.

I remember starting here as a house physician in 1951 at a time when medicine and surgery were about to make new and exciting advances. The hospital had already served this community for many years in general medicine and surgery, and pioneers such as Barney Purce in thoracic surgery, Cecil Calvert in neurosurgery, (Incidentally, a direct link in my story here — Harvey Cushing trained Hugh Cairns who trained Cecil Calvert), Jimmy Withers in orthopaedics, had made the advances into the necessary specialization to allow this hospital to keep abreast. A new generation was poised to make advances into more technical and sophisticated specialization and this happened on a broad front. Cardiology, cardiac and thoracic surgery, neurology and neurosurgery, a broadening metabolic field, emergence of clinical haematology, new surgical techniques in widespread areas, liver disease, vascular, gastric, rectal and plastic surgery, also ENT and ophthalmology. Apace with this, great advances occurred in anaesthesia, radiology and laboratory services. Deliberately I have not paid individual tributes to the pioneers as many of them are present and comments could be invidious. But I have no doubt that if one follows the history of an institution such as this hospital, the essential need for its survival and success is a questing spirit of adventure, willing to meet the new challenges of techniques and advances in medicine. Such a spirit existed in the 1950's and does so equally in the 1980's. In thinking of the excellence of this hospital's specialties let me admire gastro-enterology — for this medical school a rich field — the mechanisms of intestinal absorption, gut hormones, liver disease, surgery of the vagus and colorectal disease.

A hospital for all seasons. How does a general physician or general surgeon survive on this site in the presence of such excellent specialties? (One feels he might well come into this hospital by the back gate — and so he does — but so does everyone else!) I would argue that generalists still have a significant role in acute take-in wards and in general outpatients. It may seem strange to profess a love of the acute take-in problems in either outpatients or the ward, but here one is attempting to meet the patient on his own terms by his definition of an emergency and to provide assistance and to give an assurance that "the simple will be separated from the serious" (Pellegrino and Thomasma).

To work in medical and surgical take-in wards could easily be regarded as chore but they have their fascination. The ability of ward sisters to find beds where no beds are; the ability of casualty to cope with the flow on a busy day; the ability of the young medical and nursing staff on the wards to sort out, write up, erect drips or comfort a section of the community who are, more often than not, frail, elderly and

in various degrees of suffering. A take-in ward towards evening portrays a better flotsam and jetsam of life than any shipwreck. In the last year or so the University has concerned itself as to whether the procedures for selecting medical students are selecting the best candidates. I have no doubts, no doubts whatever, that our young medical graduates in their houseman year are as good as, or in fact better than ever. My implied praise of the general medical wards is even more true of the acute surgical wards and casualty during the last 14 years — areas in which during the stress of these years the polished skills of previous generations of general surgeons have been upheld and sustained by the present surgeons. As Sister Kate O'Hanlon — quoted in Readers' Digest — said, "You might say that some good does come out of evil".

To a slight degree I sometimes yearn for the former outpatient clinic in the old entrance hall. You could always hear and be educated by hearing clearly what was going on in the neighbouring cubicles. But fortunate we were in having a new outpatient clinic built in the late 1960's — just in fact when we needed it. It is a pleasure to express gratitude to those who originally planned with foresight this centre. It is possible to dismiss outpatient work on the basis of the Pellegrino description that "the simple will be separated from the serious". It is possible to feel that 90 per cent of what one sees is simple and beneath the effort of so much investigation. The simple is often mild psychiatric anxiety, depressive-type illness. Sir Douglas Black quotes Clemenceau in stating that "War is too serious to be left to the generals", and momentarily appears to go on to say that psychiatric illness is too serious to be left to the psychiatrists.

In actuality, what Sir Douglas said was, there is so much minor psychiatric illness that it is a load far exceeding the ability of psychiatrists to cope with, and that general physicians and general practitioners must involve themselves in this form of care. To us this task is made easier by the marvellous help of the social services of this hospital — Betty Hall's rich legacy. Sometimes one catches a view of the future of medicine which prophesies such old fashioned clinical contact with patients will be unnecessary. Dr Glen Seaborg describes the future: "For several days you have not been feeling well and you call your local health center for an appointment. At the center you give all the necessary information to a medical secretary whose typewriter feeds it into a computer system. The computer may venture an immediate diagnosis — but if it has any doubts, it recommends one or several diagnostic tests. In a matter of seconds the system presents its full diagnosis. The health center efficiently adds the day's information to your medical history and sends your doctor a copy just for the record. By the way, you do get to see your doctor — on the weekend when you play bridge with him."

There is another critical view of outpatient clinic work as being relatively useless because it concerns itself with the investigation of established disease and that it is too late. The same view is that more medical effort should be directed into prevention — a search for positive health. This is a popular belief; also a belief of media and Government. Unfortunately experience tends to show that routine head-to-toe examination, similar to a 5,000-mile car service, has a very limited usefulness in apparently healthy individuals. Perhaps because disease seldom arises on a single cause but is probably the result of a complex chain of events. More preventative medicine is undoubtedly intended to fulfill the World Health Organization definition

of health as a positive state of physical and mental wellbeing. One sceptical observation has been made that the normal state of most people is to feel faintly tired, harassed and under the weather, and that an unbounding state of positive health presages incipient hypomania. Truly useful preventive measures do happen daily in this hospital — prenatal examinations; screening of the newborn; active treatment of hypertension, rheumatoid disease and diabetes; breast biopsy and endoscopies. And if I had to define useful preventative medicine I would produce and admire the work of the ophthalmology department in screening for diabetic retinopathy.

In a hospital for all seasons would I wish to increase its efficiency by treating only the curable and by logical conclusion arranging to transfer the incurable elsewhere? Personally I think not. I hope not. At this point I had intended to say a few critical comments about some developments in the care of the dying but perhaps that would be unwise — even unfair — and my intention today is essentially to be happy and not carping. I would plead with the Death Awareness movement (American usage) or those in this country who believe in “Dying Well” to be slightly more balanced in their description of the attitudes of traditional hospitals to death of patients with incurable disease. The medical and nursing profession are often portrayed as sitting blindfolded, unintelligent, unfeeling and uncaring by the bed of the dying. It is not so and I do not believe it has been so. For instance, if you tell me that there is a system of nursing of the dying that is more caring than that given by the nurses in this hospital then indeed the angels have come down from heaven and someone has forgotten to tell us. There is nothing new about “Dying Well”. Edmund Spenser — date November 1589 — departing from County Cork with Sir Walter Raleigh for the fame of London on the publication of “The Faerie Queen”:

“Sleep after toyle.  
Port after stormy seas.  
Ease after warre.  
Death after life does greatly please”.

(And of interest, these lines were used by John Henry Biggart at the funeral service of W.W.D., another admirer of Osler.) It is appropriate to quote such a view when, as in the case of Sir William Thomson, death occurred in a man full of years and full of honour, but it is more difficult to be so philosophical with early unwarranted intrusive death. Because it is more difficult it is therefore more important that we accept the challenge.

There is nothing new about doctors being committed to the care of the patient in his terminal illness. Dr Jacob Bigelow, Boston 1858: The physician’s duties are ‘to diagnose, to initiate treatment, to offer relief of symptoms and to provide safe passage’. Having said that — perhaps too aggressively — I would acknowledge a justifiable criticism of some lack of communication between doctors and the dying. Sir Thomas More in Utopia saw the need to talk to the terminally ill: “Such as be sicke of uncurable diseases they comforte with sittinge by them, with talkinge with them, and to be shorte with all manner of helpes that may be”. Perhaps the need to spend more time, otherwise in comforting the dying by such simple endeavour as the companionship of talk is the chief lesson we must learn from the Hospice movement. My slight irritability — even unreasonableness — on this subject would be unworthy if it did not contain some principle within it. The principle I discern is that if the caring element in medicine, which is particularly evident in the care of the dying, is

separated off as a new specialty or new expertise from the main body of medicine, then that main body, as in a teaching hospital like this one, will become more and more technologic in its skills and its outlook and will be bled anaemic of compassion and charity — that charity which “suffereth long and is kind” — the Caritas of St Paul.

A hospital for all seasons sounds complacent — too complacent, I suspect, for some of the audience who are aware of a general mood of highly intelligent criticism of the medical profession by Illich, McKeown, Cochrane, Kennedy. The criticism is, largely, that the technologic nature of modern medical intervention is itself a threat to health — reduced to simple terms, Illich sees the production of dependent, helpless patients as the logical outcome of many forms of modern treatment. Other criticisms are that the medical profession has abrogated to itself excessive power, is too paternalistic, is over concerned with scientific problem-solving so that the particular of a disease is more important than the whole person. Generally, the Illich type criticisms deserve our consideration and certainly not unreasoned rejection. It was a doctor who wrote, “The greatest peril of excellence is contentment (Willis Hurst).

Because of the criticisms, would I advocate alternative medicine in my hospital for all seasons? The answer is “No” and that will be construed as a reactionary answer, but “No” is really a mild answer. Oliver Wendell Holmes, Osler’s contemporary, said of alternative medicine 100 years ago: “A mangled mass of perverse ingenuity, of tinsel erudition, of imbecile credulity and of artful misrepresentation”. In 1962, Louis Lasagna, distinguished former Professor of Pharmacology at the Johns Hopkins defined certain characteristics of cults or alternative medicine. Firstly, cults are advocated by articulate people. Secondly, after a time any cult will attract famous and apparently intelligent people. Finally there is a standard rebuttal of criticism: “They persecuted Galileo, too, didn’t they?” In the 20 years since Lasagna’s views, the criticisms of traditional medicine of Illich and others have appeared and alternative medicine has enthusiastically incorporated these criticisms into its philosophies, unfortunately also aided by the media who now regard as profitable copy a harlequinade of Illich views and a gullible endorsement of alternative medicine; all of this without any regard to the vulnerability of the public mind on matters of health. At the dawn of scientific medicine, 1628, William Harvey, discoverer of the circulation of the blood, said, “It were disgraceful with this most spacious and admirable realm of nature before us, where the reward ever exceeds the promise, did we take the reports of others upon trust”. On the road we have travelled since 1628 — Addison and Bright, Graves and Corrigan, Banting and Salk, smallpox, poliomyelitis, diabetes, pernicious anaemia, Hodgkin’s disease. “The reward has ever exceeded the promise”. Any arrogance in my attitude is limited by the knowledge of the imperfection of medical progress in many other diseases. I hope I have not put too much emphasis on the inherent incompatibilities of traditional and alternative medicine because our real problems are elsewhere. How, with finite resources can we provide care for the elderly and chronically ill and also afford the costly technology used in many acute diseases?

In thinking of Osler’s textbook, written while he was in America, I am conscious of the influence of a succession of medical textbooks from the USA — Cecil and Loeb, Beeson and McDermott, and Harrison — which seemed wider in scope and more philosophic than the textbooks produced within these islands. It is a great

pleasure to note that at last a new British textbook of medicine has appeared from Oxford (Osler's final home) which has some of that trans-Atlantic sparkle and commonsense and a feeling for the patient that is refreshing. Listen to the opening chapter quoting the work of Professor Ronald Girdwood, now President of the Edinburgh College of Physicians. (This College has been kind particularly in its several visits to Ulster over the last decade). The problems facing a new patient in hospital (abbreviated version):

“Away from home, perhaps for the first time.

Confined to bed; a strange high bed; surrounded by patients in other beds.

Clothes are taken away; given strange backward gown to wear.

Cannot come and go as one pleases.

Cannot select own food.

Cannot take own bath.

No privacy; must submit to examination by any and all who desire.

Can't sleep for the noise of nurses working in the early hours of the morning.

The doctor in direct charge is too young, and the older ones are too busy to listen to my long story.

Life is made a misery by medical students using me as a guinea-pig for practising taking of blood, etc.

I'm not a person, I'm just another case”.

I am sure Osler would have bowed in acknowledgment of that commonsense description of a patient's emotions and would have advised us to consider it in our daily work.

The Royal Victoria Hospital — a hospital for all seasons. Does the Department of Health and the Eastern Board think it is a hospital for all seasons? I wonder if they do? Dr Oliver thought so and told them so, that we were a hospital for all seasons but instead of heeding that view we continue to be regarded, I suspect, by them as a problem for all seasons. Hegel's view, that what history teaches us is that men have never learned anything from it, certainly applies to the history of successive re-organizations of the Health Services. Nineteen hundred years ago Petronius, a Roman consul, wrote, “We trained hard . . . but every time we were beginning to form up into teams, we would be re-organized. I was to learn later in life that we tend to meet any new situation by re-organizing . . . and a wonderful method it can be for creating the illusion of progress while producing inefficiency and demoralization”. Petronius has a remote Irish connection. The chief translator of his poems was Helen Waddell, Fisherwick Church, Victoria College, and much else besides. Sadly, it is now proposed that a happy brotherhood between ourselves and the Mater Infirmorum Hospital is to be severed. Bishop Cahal Daly said recently: ‘The most precious contribution the Mater can make to the Health Services is precisely its tradition, its spirit, its ethos’. Personally I am sad that a close co-operation between the Royal and the Mater should now be terminated by edict. The very close relationship of the last ten years between this hospital and the Mater was not only good for both hospitals but it was good for medicine in Ulster and it was also good for Ulster.

Although five centuries separated Thomas More and William Osler, they had much in common. Both have been described repeatedly as humanists. Humanism has been defined as a system of thought or action which assigns a predominant



interest to the affairs of men as compared with the supernatural or abstract. I had started with Christina Rossetti's prayer to emphasize that the humanist knows he approaches his task in stumbling walk and scant measure. In 1970, Wilder Penfield in a symposium based on Osler's life entitled "Humanism in Medicine" said: "The art of the practice of medicine is a spiritual matter and so we would do well to listen to the voice of Osler". It is difficult to summarize Osler at an interval of more than 60 years since he died. He was fortunate in the times he lived in. About the turn of the 19th century it has been said, "A random patient with a random disease consulting a doctor chosen at random had for the first time in the history of mankind a better than fifty-fifty chance of profiting from the encounter". He was fortunate in his biographer Harvey Cushing, who certainly described Osler as all virtue and no blemishes, but allowing for all of this he seems to have been a very unique man. The acknowledged greatest clinician of his age, a thinker with great compassion and charity, a man with a sense of the history of his profession, a great leader of the profession.

It is traditional, in ending, to give some advice to the students about their undergraduate careers, but I have already indicated a limitation on advice from one generation to another. I have a simplistic ideal that those taking up medicine should simply want to be doctors and when they are doctors, to occasionally reflect how fortunate they are in having the privilege of belonging to a profession that is, in Osler's phrase, "a way of life". Osler would have been able to say much to them, but his main advice would have been to echo Thomas Sydenham's advice to a youth from Killyleagh, Hans Sloane, "You must go to the bedside. It is there alone that you can learn disease".

The concept that wanting to be a doctor would be sufficient can be easily ridiculed and yet life is continually full of images and a recent lasting image is of Dr David Greer, medical student and later house physician, Wards 9/10 and later Wards 1/2, working for medical examinations up to the last few weeks of his rapidly developing fatal illness — working on in the full knowledge that the night was coming. I have also a memory of Richard Wormersley in near tears as he watched these events, and that is what my recall of Osler is all about.

To an extent that is why the story is important because it focusses on ageless and, I think, changeless attributes necessary for the practice of medicine. Commitment and caring, and the joy of being a doctor or a nurse or a member of the greater medical profession. I have no doubts that these virtues endure in this hospital and that the drum beats of medical destiny beat in the wards and operating theatres of this hospital — the Royal Victoria Hospital — as they did and do in the Johns Hopkins. I am entirely optimistic about the future of medicine and this hospital, and greatly happy to have spent the greater part of my life within its walls. On 7th July 1535 that man — Sir Thomas More — mounting the scaffold said, "I pray you Master Lieutenant see me safe up". I pray you Master Willoughby, see me safe up — and out of here soon.

Thanks are due to Miss May Weller for her help, and my wife and Dr Terence Fulton for helpful comments; also the Medical Library staff and Archivist's Office, for a certain amount — perhaps a good deal — of patience and forbearance.

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# **A RECIPE FOR TRANSPLANTATION**

by

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**The Scott-Heron Lecture, 1983**

I am greatly honoured to be invited to give the Scott-Heron Lecture for 1983 but feel very inadequate to follow the distinguished doctors who have preceded me.

The interest in the kidney was first aroused by a young woman with bilateral staghorn calculi, while working as a house surgeon with the late Mr. Cecil Woodside. Mr. Woodside was a general surgeon who had a special interest in the kidneys and particularly in renal stones. He removed huge stones from kidneys of the patient, Mrs. Brigid Kelly. Later when they recurred in the left kidney he carried out a left nephrectomy. I am glad to say that the stones did not recur in the remaining kidney and Mrs. Brigid Kelly still remains well with excellent kidney function at the age of 70. Mr. Woodside was greatly interested in the pathogenesis of kidney stones and encouraged me to continue my interest which led eventually to the formation of the Renal Unit at the Belfast City Hospital in 1959.

I cannot describe this work without acknowledging the help, encouragement and support of my husband, Max Freeland. Dr. Terence Fulton in a kind tribute to him at the Opening Address in October 1982, commented on the helpful influence he had exercised on generations of medical students. I met him just before I graduated and the help, encouragement and support which I received from him is beyond estimation.

The work which I will describe belongs to the whole team associated with the Renal Unit of the Belfast City Hospital. The whole project depends on the able and devoted work of the nursing and technical staff in equal measure with that of the medical members of staff. Moreover we are greatly helped by the support of the laboratories, radiology, indeed the whole of the medical support services. Not only this, but the work would be impossible without the co-operation of the intensive care units in other hospitals. We owe a particular debit to the Respiratory Intensive Care Unit and the Neurosurgical Unit of the Royal Victoria Hospital.

It was shown by Ullman in Vienna as long ago as 1902 that the kidney of a dog could be transplanted from its normal site into the neck and urine would be produced, demonstrating that the kidney did not require a nerve supply. He was able to demonstrate that a kidney from another dog, or even from a goat would also produce urine in the new host but does not appear to have carried his experiment further. Carrell, also in Vienna, in 1902 confirmed Ullman's observations and went on to transplant a kidney from a dog to a bitch, removing the bitch's own kidneys, and the bitch remained well with good kidney function for some days but ultimately the graft ceased to function. Williamson carried out a similar experiment in 1923, and his description of the appearance of the kidney graft provides a classic description of rejection.

Transplantation of human kidneys was attempted in Boston from 1951 onwards, using "free" kidneys or cadaver kidneys. In 1954 Murray and Holden reported four human cadaver grafts, three of which failed but one survived, apparently without using immunosuppression. In the meantime research into the nature of the rejection process had revealed that it ought to be possible to transplant kidneys between individuals whose genetic similarity was sufficiently close, without fear of rejection. This led to the first transplantation between identical twins in Boston in 1954. This operation was successful, and over the next five years transplantation of kidneys between identical twins was carried out in a number of centres in Europe and America. Some of these transplants failed for technical reasons but in none of them was there any evidence of rejection. It is obvious that few patients reaching end stage kidney failure are fortunate enough to have an identical twin, able and willing to provide a kidney. This led to research into how rejection might be prevented when the graft came from a less closely related individual.

In 1958 it was shown by Hamburger in Paris that whole body irradiation would prevent rejection of the grafted kidney, but it almost invariably led to death of the patient because of bone marrow depression followed by uncontrollable sepsis. Research then centred on the possibility of preventing rejection by a drug, or drugs, in the hope that this could be controlled more easily than was whole body irradiation. At the beginning of the 60's Murray and Calne in Boston used 6-mercaptopurine in dogs and found that while it was immunosuppressive it was also very toxic. Burroughs-Wellcome in New Jersey produced an analogue of mercaptopurine, azathioprine, which proved in dogs to be a good immunosuppressive, as well as much less toxic, drug. In 1962 azathioprine was used successfully to prevent rejection when a kidney taken from a patient dying during an open heart operation was transplanted into an unrelated individual. Despite several rejection episodes the kidney continued to function for two years. About the same time cyclophosphamide and actinomycin were given to prevent rejection but proved to be more toxic than azathioprine, which thereafter became generally accepted as the drug of choice for kidney transplantation.

Goodwin in 1962 reported that corticosteroid reversed rejection a number of times in a mother-to-child graft being treated with cytoxan (a drug similar to cyclophosphamide). Thereafter although their mode of action was unknown, and possibly mainly only anti-inflammatory, steroids were given along with azathioprine as the standard immunosuppression for kidney transplantation. Later attempts were made to develop a more specific weapon, antilymphocyte serum, against the small lymphocytes which infiltrate rejecting grafts. Antilymphocyte serum produced very promising results in animals but has been disappointing in human clinical transplantation. It is difficult to produce and standardize a satisfactory serum, and the use of antilymphocyte serum or globulin is still controversial even today.

Another factor which contributed greatly to the development of kidney transplantation was the invention of the Scribner shunt. This made it possible to use the same blood vessels for repeated treatments by the artificial kidney, so that a patient could be maintained for long periods, with improvement in general condition, until a kidney became available. This was later superseded by the arteriovenous fistula first suggested by Brescia in 1966. The discovery of the Scribner shunt in 1961-62 inevitably led to an interest in treating patients with chronic renal failure in those

units originally set up for the provision of treatment of acute renal failure. This happened in Belfast where patients were sometimes referred with renal failure of acute, or apparently acute onset, which in fact was due to irreparable kidney disease. In Belfast the earliest attempt to use a Scribner shunt was made in 1964 with the help of the late Mr. Megaw, and by the beginning of 1965 a patient was being successfully maintained, using the available facilities intended for treatment of acute renal failure.

In 1965, the DHSS in London called a meeting of those people already using haemodialysis, to decide whether the time had come to provide regular dialysis therapy for end stage renal disease. This was followed by the setting up of a Working Party with the brief of setting up a centre for regular haemodialysis therapy in each hospital region.

From the time of Murray and Calne's discovery that cadaveric transplantation was possible with the aid of azathioprine, it seemed that transplantation would prove eventually to be the way to replace kidney function but that good quality dialysis therapy was necessary to make the patients fit and maintain them until kidneys could be provided.

As a preliminary stage to setting up a kidney transplantation service here, occasional patients were sent to centres already transplanting in other parts of the United Kingdom, a form of "transplant brokerage." Over the years 1962-1968, 17 patients were "sold" to colleagues, most frequently to St. Mary's Hospital or to Roy Calne in Cambridge. Three of these patients are still alive, the longest one with a cadaver kidney still functioning excellently after 18 years, one of the longest in Europe.

During these years I was actively trying to obtain what I regarded as the minimum facilities for renal transplantation. The need for dialysis had already outgrown the small promises in Ward 9 even without transplantation. The late Mr. Megaw had generously allowed the use of a cystoscopy theatre for a 2-bed regular dialysis service and four patients were maintained without any additional medical staff and little in the way of equipment. By 1964 it was envisaged that the renal service would develop in the new Tower Block but in the meantime it was apparent that more space was needed. It became clear that the only way this could be provided was by the so-called "temporary" building now known as Renal I. In the meantime the Working Party of the DHSS had recommended the provision of a 10-bed dialysis unit for each hospital region, but the planning of our 6-bed unit to provide for acute renal failure and a small amount of treatment of chronic renal failure by dialysis and transplantation, was already at an advanced stage. It was decided to proceed with the original plan, providing the 10-bed haemodialysis accommodation as a second phase (which was ready for use by May 1972).

The first phase of the building was ready for occupation in July 1968, the part now known as Renal I. This contains 6 single rooms, a theatre and a 2-bed dialysis room, plus the usual offices (Figure 1). The unit differs very greatly from an ordinary ward. The individual patient rooms are situated between "clean" and "dirty" corridors, communicating with each. Entry of staff is via changing rooms as to a theatre suite, and all medical and nursing care is provided via the "clean" corridor. Disposal of all used items is via pass-through cupboards to the "dirty"

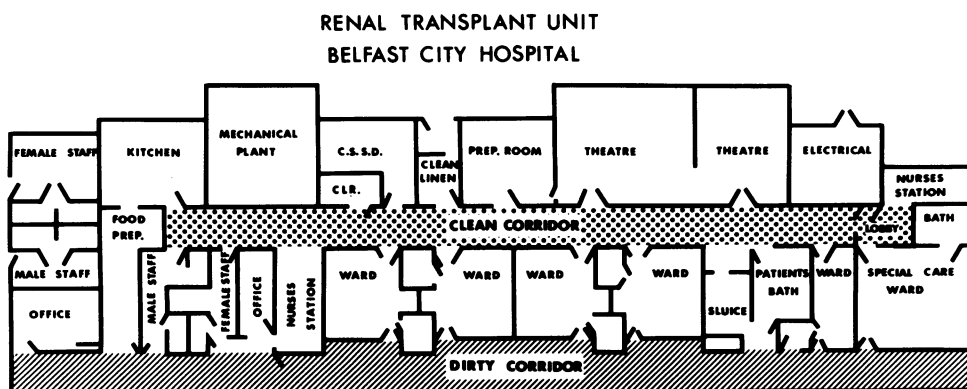


FIG. 1  
*Plan of Renal 1, Belfast City Hospital.*

corridor. Each room has its own air supply and differential pressure ventilation ensures that air flows from "clean" towards "dirty" areas. This system provides good quality reverse barrier nursing, without the need for air locks, provided that the discipline of usage is properly carried out. This design allows the use of the unit to treat both patients with recent transplants as well as patients with acute renal failure who may be infected.

During the early part of 1968, with my colleagues, the plans for renal transplantation were worked out in detail. The legal aspects of transplantation were explored with the Legal Advisor of the Northern Ireland Hospital's Authority, and with the Belfast Coroner, the late Dr. Lowe.

A major part of the work of these meetings was the formulation of the recipe for transplantation (Table I). The recipe differed radically from the practice in the already established centres for transplantation in Europe and the United States. In 1968 most centres preferred to use living related donors rather than cadaver donors, and results of transplantation were vastly better using living donors. As the organization for cadaver donation is more complex we decided to prepare ourselves for the more difficult task. Our planning therefore provided for the additional problems related to the harvesting of cadaveric kidneys. We accepted the probability that most of the transplanted kidneys would develop acute renal failure, rather than functioning immediately as do most living related kidneys. The fact that post-operative haemodialysis would be needed did not seem to be a serious complication, which leads me to the next point, the organization of our clinical team.

In the establishment centres the transplantation service was entirely in the control of surgeons. Patients awaiting transplantation were maintained by regular dialysis therapy under the care of nephrologists. They carried out the investigations of family members in search for a living donor but took no part in the location of cadaveric donors. Once the patient entered the transplant unit the nephrologist relinquished all responsibility to the surgeons. One consequence was that should

TABLE I  
*Recipe for Transplantation*

- 
1. Cadaveric donors.
  2. Organization of clinical team.
  3. Preparation and assessment of recipient
    - (a) bilateral nephrectomy
    - (b) blood transfusion.
  4. Tissue matching.
  5. Transplant operation
    - (a) anaesthesia: consultant
    - (b) surgery
    - (c) per-operative transfusion and IV therapy
    - (d) avoidance of unnecessary drugs.
  6. Immunosuppression.
  7. Prevention of infection.
  8. Caution in diagnosis of rejection.
  9. Long-term follow-up.
- 

post-operative haemodialysis be required this was carried out by doctors without experience in the management of acute renal failure.

Our plan envisaged transplantation based on a closely integrated team of nephrologists, surgeons, anaesthetists and the tissue matching service. The nephrologists were to prepare and assess the recipient providing full information for the surgical team who were to be briefed in advance of any special problems. This approach later paved the way for transplantation in patients without adequate bladder function, using an ileal conduit, and in diabetics. In 1968 it was only feasible to use ABO matching for distribution of kidneys. Such tissue typing as was then possible took longer than it was considered safe to keep the donor kidney so that the tissue typing result became available only after operation, and therefore was of academic interest only.

The surgical team prepared their techniques by carrying out a series of transplants in dogs. This was to provide practice in removal and perfusion of donor kidneys as well as of insertion of kidneys. A surgical technician was available to help with the perfusion of kidneys. The surgeons were responsible for drawing up lists of instruments, etc. required for the donor trays and the transplant operation trays. The Renal Unit theatre sister was to be responsible for their packing and sterilization. Special containers were made for the donor instrument trays, sterile perfusion fluid and sterile plastic bags to contain the perfused kidney, which were to be taken to the place where the donor operation was to be carried out, of course with full aseptic precautions. A supply of ice chips in which to pack the kidney in its plastic box, had to be arranged.

The nephrologists undertook the role of organization for procurement of donors, one of them being always on-call by bleep or by phone, to discuss with the doctor who was offering the donor the suitability and logistics of harvesting the kidneys. In due course the surgeon on-call was contacted and proceeded to harvest the kidneys

as soon as possible. The surgical team was responsible for all aspects of perfusion and chilling of the kidneys. In the meantime the nephrologist was to decide which recipient should receive the kidney, in 1968 on the basis of ABO identity and chronological order, also bearing in mind clinical need. At this stage only one kidney could be used locally and there was as yet no method of sharing kidneys, although we were able to take part in a kidney-sharing scheme, "The London Transplant Club," by 1971.

The availability of our dedicated theatre facilitated the operation at a time when it was thought unwise to keep a kidney chilled for longer than 4 hours. The anaesthetists had previously agreed about the type of anaesthesia and agreed to provide a consultant on-call rota so that expertise was gained at the maximum possible rate. During the operation the nephrologist on duty prepared the immunosuppressive drugs, and was to be available throughout to advise on blood requirements and drugs, and arrange details of early post-operative care.

The post-operative care was to be mainly the responsibility of the nephrologist who would prescribe all drugs used, to prevent confusion arising. The surgeon would be responsible for care of the wound itself, and the period of time for which wound and catheter drainage was required.

It can be appreciated that the nephrologists, from the very beginning, played a prominent role in the transplant situation. It is interesting to note that now in the 80's almost all transplant teams include one or more nephrologists. It must be admitted, however, that they do not usually play as prominent a role elsewhere as in Belfast.

Most patients awaiting transplantation are supported by dialysis but occasionally transplantation may be carried out just before dialysis becomes essential. Each body system must be carefully assessed so that problems may be anticipated. Hypertension must be controlled. When hypertension is not controlled by dialysis with the minimum of drugs bilateral nephrectomy is usually carried out. The original protocol provided for bilateral nephrectomy for all recipients, for control of hypertension, and removal of a source of potential infection or tumour. Although with time and increase in workload this policy had to be abandoned and bilateral nephrectomy used more sparingly, the bilaterally nephrectomized recipient is easier to manage in the early post-operative period. There is no uncertainty about the source of any urine passed, all of which must come from the new kidney. A late benefit of bilateral nephrectomy is the very low incidence of hypertension, compared with patients retaining their own kidneys.

Blood transfusion is worth some detailed consideration. The anaesthetists were perturbed about the marked anaemia of most patients with end-stage renal failure. It was agreed by the team that all patients should be given transfusions to prevent symptoms of anaemia. The need for transfusion was increased by the policy of bilateral nephrectomy. Now about the time we were planning transplantation, hepatitis B began to appear in renal units in other areas and transfusion came to be regarded as potentially dangerous to staff and patients. It was discovered also that some patients responded to transfusion by developing antibodies against antigens in the transfused blood. There developed a strong body of opinion that patients awaiting transplants should not be transfused, this despite evidence from transplants



that transfusion improved graft survival. We considered many times from 1970 onwards whether we should discontinue blood transfusion, but as we were obtaining good graft survival decided to continue to transfuse, albeit somewhat more sparingly. In 1973 Opelz and Terasaki reported that graft survival was better in transfused than in non-transfused patients. This report was criticized on the grounds that it contained data from a large number of centres, but over the next few years experiments in rodents, dogs and rhesus monkeys all suggested that prior transfusion led to improved graft survival although admittedly hyperacute rejection occurred in some animals. Gradually the evidence accumulated in human transplantation that transfusion improved graft survival, and this is now generally accepted.

Tissue matching, apart from ABO, played no part in the early disposition of grafts as it was available only retrospectively. Nevertheless, graft survival was good from the beginning. Although we now prefer to obtain a 2 (out of 4) antigen match or better, this is because it makes it easier to carry out a second or even third graft should this become necessary. Regular checking for cytotoxic antibodies was added to the programme later.

To return to the recipe: The importance of high quality anaesthesia can not be over-emphasized. Until quite recently all anaesthetics for transplantation were given by consultants. Problems with anaesthesia have been remarkably few despite the fact that many of the patients have ischaemic heart disease of serious degree and all are anaemic. It is important that the blood pressure should be kept slightly high, in the range usual for these patients, and must not be allowed to rise unduly or fall.

Time does not permit me to go into the details of the operations for removal and insertion of the donor-kidney. For those unfamiliar with the subject the kidney is inserted into one or other iliac fossa, using the internal or external iliac vessels for vascular supply. The ureter is joined by one of several methods into the bladder lying conveniently near. Problems with the vascular anastomoses are relatively rare despite the fact that none of the surgeons have training in vascular surgery. Surprisingly, complications related to the ureter, including urinary leakage, sloughing of the ureter and late stenosis are fairly common. In Belfast, but in relatively few other centres, a capsulotomy along the convex border of the kidney is carried out routinely to help prevent rupture of a kidney swollen by acute tubular necrosis or rejection.

Great care is taken over the fluid balance during operation and post-operatively. Electrolyte fluids are given in small amount at the beginning of operation to permit administration of anaesthetic and immunosuppressive drugs. Thereafter blood loss is replaced generously with whole blood. It may be important that all unnecessary drugs are avoided. We do not give mannitol, frusemide, anticoagulants, prophylactic antibiotics or anti-fungals, although many other centres use them.

The immunosuppressive drugs are of crucial importance. In 1968, as indeed today, there was no general agreement about immunosuppression. A list of immunosuppressive therapy then in use is shown in Table II. It seemed to us best to commence with the simplest method, using azathioprine and steroid only, but the problem was the dosage. I obtained the protocols from St. Mary's and Cambridge, both of whom had successfully transplanted my patients. Cambridge used much

TABLE II  
*Immunosuppression in use in 1968*

- 
1. Lymphatic duct drainage.
  2. Irradiation of graft.
  3. Azathioprine.
  4. Azathioprine plus steroid.
  5. Antilymphocyte serum.
- 

TABLE III  
*Immunosuppression for Renal Transplantation (Belfast Regimen)*

---

Initial immunosuppression:  
 Imuran 5 mg/kg body weight—slowly;  
 Hydrocortisone 200 mg;  
 (given intravenously as soon as possible after intravenous infusion is commenced).

Remainder of first 24 h:  
 No further Imuran;  
 Hydrocortisone 200 mg given intravenously at 0 + 6, 0 + 12 and 0 + 18 h.

Maintenance immunosuppression:

- (a) No significant function;  
 Imuran 1.5 mg/kg body weight daily;  
 Prednisolone 20 mg daily.
- (b) Creatinine clearance of 30 ml/min or greater;  
 Imuran 3 mg/kg body weight, given as a single dose;  
 Prednisolone 20 mg daily for first 6 months. Dose is gradually reduced thereafter to 10 mg daily,  
 if there are no signs of rejection.

Anti-rejection therapy;  
 Prednisolone 200 mg, reducing in 3 or 2-day steps through 150, 100, 75, 50 to 20 mg per day.

NB: Extreme care is taken in making diagnosis of rejection.

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more steroid than did St. Mary's who gave larger doses of azathioprine. It was decided to use the lower dose of both drugs. St. Mary's were then giving 10 mg of prednisolone twice daily from the second 24 hours onwards, whereas Cambridge gave 75 mg daily until diuresis occurred. It was only some years later that I discovered that St. Mary's increased their dose of steroid soon after I contacted them, because of unsatisfactory graft survival. The dosage we used at the beginning is shown in Table III. The initial maintenance dose of prednisolone was 10 mg bd but was reduced much more gradually than in St. Mary's, using three month steps.

As it seemed more logical to give the steroid as a single morning dose as being less likely to lead to adrenal suppression, this policy was followed from the third patient onwards. No other changes have been found necessary. The much lower dose of steroid given in Belfast compared with other centres is shown in Figure 2, where the area under the curve gives the total dose. It should be remembered that these are maintenance doses, patients in whom rejection occurs receive much more.

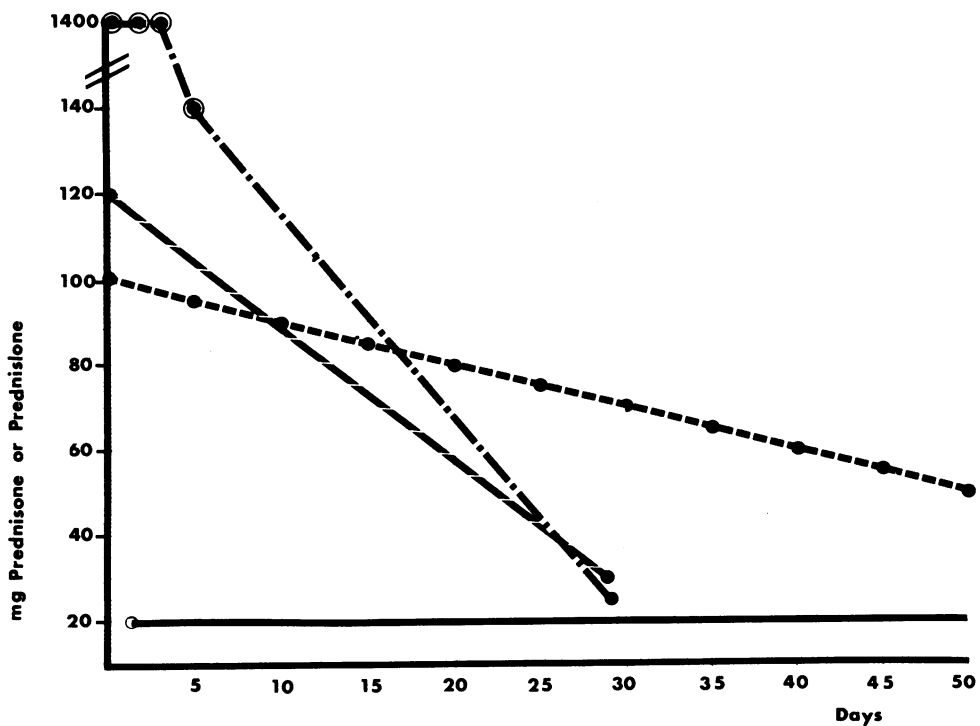


FIG. 2

*Cumulative actuarial survival curves for survival of first cadaver grafts in UK centres.*

Moreover, some of the centres illustrated combine this therapy with antilymphocyte globulin, local irradiation of the graft, sometimes splenectomy or lymphatic duct drainage, all of which carry their own hazards.

The gratifying fact is that in the 80's transplant centres all over the world have reduced their dosage of steroid, encouraged by our good results using such relatively low doses, although many still use more than we give. Our own experience, and research, strongly suggests that in many patients even lower doses than we use may be sufficient.

I do not have time to consider treatment of rejection in detail but it is not remarkably different from that in use elsewhere. The dose of prednisolone is increased to 200 mg daily reducing in 3 day steps through 150, 100, 75 and 50 mg back to 20 mg daily. We originally gave a single intravenous dose of actinomycin C but this was not obtainable after 1972 and no other drug was given in its place.

The seventh point in the recipe is the prevention of infection. This seemed very important because the commonest cause of death following transplantation was then, and still is in many centres, infection. The majority of the infections appeared to be due to the usual types of hospital organisms though it was becoming clear that

TABLE IV  
*Toxic effects of Steroid Therapy encountered in Belfast*

TOXIC EFFECT	No. OF PATIENTS
Death from infection	5
GI perforation	2
Haematemesis	5*
Diabetes mellitus	7
Avascular necrosis	4
Osteoporosis	5
Cushingoid	7
Overweight	89
Posterior polar cataract	12
Total patients	220

\*1 death

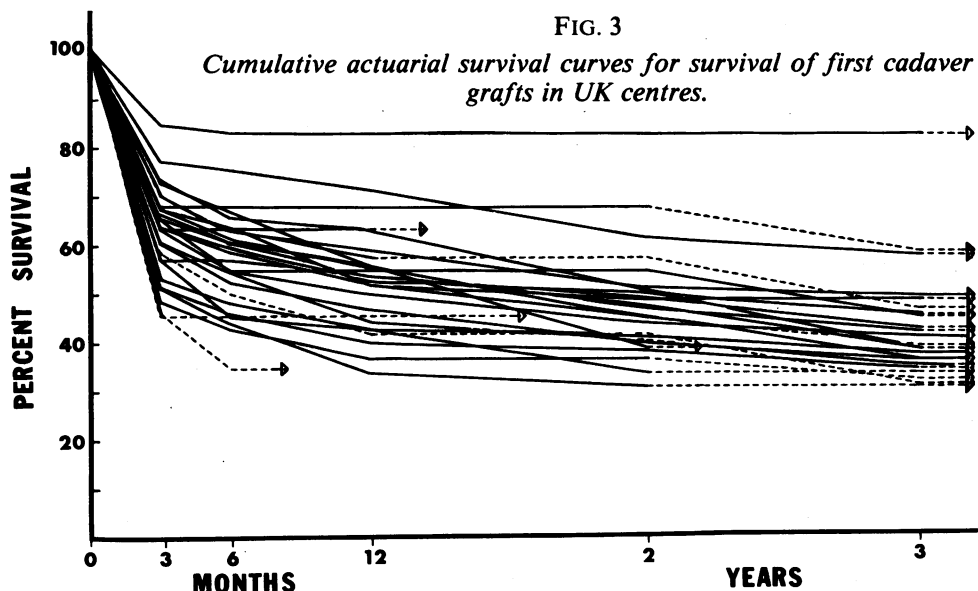
unusual infections may occur. The known high incidence of hospital infections dictated the design of Renal I, illustrated in Figure 1. The design certainly provides protection but the sparing use of steroid may be of at least equal importance. Table IV shows the steroid-related complications encountered in the first 220 patients transplanted. Only five patients died from infection, only two of whom died during their first admission. It is of some interest that of the rarer infections commonly reported in association with transplantation we encounter cytomegalovirus, candida and herpes frequently but without fatalities, there has been one case of pneumocystis and two of tuberculosis. None of the rarer infections known to occur in immunosuppressed patients have been seen.

The cumulative survival curves for first cadaver grafts, produced by the UK Transplant computer is shown in Figure 3. Each curve represents the results of one unit and is anonymous except to the unit concerned. The top line represents the Belfast results. These results have held through 14 years for 297 kidney grafts.

Finally, the normality of our patients is noteworthy. At least 20 of the male patients have fathered children and 6 of the women have had normal babies by the vaginal route. One patient completed the Belfast Marathon in 1982 and 1983.

The recipe used in 1983 differs very little from the original of 1968. The main difference is that tissue matching is now a pre-operative procedure, permitting matching of donor with recipient. The sharing of donor kidneys through the UK Transplant Service, and with Eurotransplant and Scandiatransplant, facilitates good tissue matching. On the surgical side improved kidney perfusion with modern perfusion fluids has meant that many kidneys now function immediately and almost no kidneys fail altogether to function.

Future improvements in kidney transplantation will depend on better methods of immunosuppression. Already another immunosuppressive drug, cyclosporin A, is being widely used but as yet the serious side effects associated with its use suggests that it is too soon to change our recipe for immunosuppression.



## 2. ALL N.O.M.D.S. CENTRES

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# PRIMARY SCLEROSING CHOLANGITIS

by

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PRIMARY sclerosing cholangitis is a rare disease of unknown aetiology in which progressive obliteration of the extrahepatic and often also the intrahepatic bile ducts occurs. Delbet<sup>1</sup> is generally credited with the first case report in 1924 and there are still only 100 cases in the literature.<sup>2</sup> The association with ulcerative colitis is well known.<sup>3</sup> We report twelve cases of primary sclerosing cholangitis seen and followed up at the Royal Victoria Hospital during an eighteen-year period (1964-1982).

## DEFINITIONS

The term 'primary sclerosing cholangitis' is used to describe non-traumatic benign fibrosis of the bile ducts causing thickening of the wall with consequent narrowing of the lumen. In recent years considerable controversy has arisen over the criteria to be used in diagnosis. The most stringent are those of Myers and his colleagues<sup>4</sup> who list the following essential features: (1) progressive obstructive jaundice, (2) absence of biliary calculi, (3) no prior biliary surgery, (4) generalised thickening of the walls of the bile ducts, (5) the exclusion of cholangiocarcinoma by a long follow-up period, (6) no evidence of primary biliary cirrhosis on liver biopsy, (7) the absence of associated diseases such as ulcerative colitis, Crohn's disease and retroperitoneal fibrosis. However, others consider that these criteria are too rigid<sup>5</sup> and may result in some true cases of sclerosing cholangitis being missed.<sup>5, 6</sup> Dilatation of intrahepatic ducts, which usually occurs above traumatic strictures, is seldom seen in sclerosing cholangitis.<sup>7</sup> Exclusion because of the presence of gallstones may prevent consideration of cases in which stones have formed secondary to sclerosing cholangitis.<sup>6</sup> Cholangiocarcinoma may also pose a problem. Duct biopsy has been recommended<sup>6, 8</sup> but well differentiated cholangiocarcinoma may have a low degree of malignancy and it may be difficult to distinguish the histological features from those of benign cicatrization. Prolonged survival can also occur in patients with cholangiocarcinoma while conversely some patients with primary sclerosing cholangitis die within a few years of the onset of the disease.<sup>5, 6</sup>

It is generally agreed that patients with ulcerative colitis, retroperitoneal fibrosis and Riedel's thyroiditis should not be excluded from consideration as these conditions may be part of the same disease process.<sup>5</sup>

The criteria used in the twelve patients in this series have been the presence of diffuse or segmental sclerosis of the bile duct that could not be attributed to gallstones or previous biliary surgery, the exclusion of primary biliary cirrhosis by serological tests and where possible liver biopsy, and of cholangiocarcinoma by a reasonably long period of follow-up.

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## DIAGNOSIS

### *Clinical Features*

Ten of our twelve patients were male. The average age at the onset of symptoms was 42.5 years with a range of 19-69 years. The initial symptom in eight patients was abdominal pain which in four was typical of biliary colic. Two of the remaining four patients experienced a dull ache in the epigastrium and in the other two it was felt in the right upper quadrant. In three patients the initial symptom was obstructive jaundice with dark urine and pale stools while one patient experienced only pruritus. When the diagnosis of primary sclerosing cholangitis was confirmed, eleven patients had obstructive jaundice and in four of these the liver was slightly enlarged. Eight patients had pruritis, three had diarrhoea and in two weight loss was a major symptom.

In five patients a diagnosis of ulcerative colitis had been made on the sigmoidoscopic, radiological and histological findings four to ten years before the symptoms of sclerosing cholangitis commenced. One patient suffered from Raynaud's phenomenon and another was diabetic. One patient had several attacks of acute pancreatitis during the ten years prior to the diagnosis of sclerosing cholangitis and required drainage of a pseudocyst. One patient had a cholecystectomy four years before the diagnosis of primary sclerosing cholangitis was made. No gall stones were found but the operative cholangiogram showed slightly irregular extrahepatic ducts. One patient had a cholecystostomy when definite evidence of primary sclerosing cholangitis was demonstrated by the operative cholangiogram. One patient had required a laparotomy and cholecystostomy for a biliary leak following a diagnostic percutaneous needle liver biopsy.

One patient had a sister with ulcerative colitis, the father of another had pernicious anaemia and the mother of a third had diabetes mellitus.

### *Laboratory Investigations*

All patients had a normal haemoglobin (mean 13.3 g), the W.B.C. was elevated in only three patients and in none was there eosinophilia. Erythrocyte sedimentation rate was raised in eight patients (mean 45 mm/hour Westergren). Serum bilirubin was elevated in eleven of the twelve patients (range 8-188 micromols/l; mean 63.3 micromols/l). There were minor increases in AST and ALT in all patients (AST range 44-173 U/l; mean 97 U/l). However, the predominant biochemical abnormality was a high serum alkaline phosphatase, present in all but one patient when first seen, the range being 125-1545 with a mean of 460 units/l (normal range 35-105 units/l).

Initial serum IgG and IgM levels were normal in all seven patients in whom they were estimated but six patients had elevated IgA levels (range 4.4-5.9 g/l, mean 4.80 g/l). Serum protein electrophoresis showed slightly reduced albumin in two patients, normal alpha<sub>1</sub> and gamma globulin levels, minor increases in alpha<sub>2</sub> globulin and an elevated beta globulin level in half the patients. Tests for antinuclear factor, smooth muscle antibody, antimitochondrial antibody, LE cells and Australia antigen were negative in all patients. Blood culture was repeatedly positive in one patient with recurrent cholangitis in whom *Klebsiella* were grown on culture.

Liver biopsy was carried out in five patients and features were suggestive of large duct obstruction with chronic inflammatory cell infiltrates. Some bile ductule reduplication was noted in two of the biopsies.

### *Radiology*

The diagnosis of primary sclerosing cholangitis was made by percutaneous transhepatic cholangiography in nine patients, the typical narrowing and beading with segmental strictures being found. In one patient the diagnosis was made by ERCP which was unfortunately followed by ascending cholangitis. In the remaining two patients the lesions were demonstrated by operative cholangiography. Intravenous cholangiography was attempted in seven patients but only in one was the biliary tree satisfactorily visualised.

## **TREATMENT**

### *Surgical Management*

In two patients T tube drainage of the common bile duct was carried out prior to referral for definitive surgery. One patient underwent Longmire's procedure of left hepaticoduchojejunostomy. Four years later a distal splenorenal shunt was performed for portal hypertension and two years thereafter she required excision of a cystadenocarcinoma of the ovary which caused her death one year later. The other patient had a hepaticoduchojejunostomy (en-Y) and the anastomosis had to be refashioned four years later. Apart from four bouts of mild ascending cholangitis he has remained well on 10 mg of prednisolone daily. A further patient with a localised stricture of the common bile duct underwent a choledochoduodenostomy. This also required to be refashioned ten years later and apart from one attack of ascending cholangitis, he has remained well on 10 mg of prednisolone daily. Portal hypertension developed in four patients, one of whom required a distal splenorenal shunt for bleeding varices four years after the diagnosis of primary sclerosing cholangitis.

### *Medical Treatment*

Eleven patients were treated with prednisolone, usually beginning with 15-25 mg per day, the dose then being gradually reduced to a maintenance level of 5-10 mg per day. Response to steroids was usually good with rapid clinical and biochemical improvement. One patient was also given azathioprine for a short period. Three patients received short courses of cholestyramine for pruritus with some improvement.

### *Side Effects*

Three patients developed back pain due to osteoporosis and one suffered compression-collapse of a lumbar vertebra. Muscle wasting also occurred in these three patients. Two patients became hypertensive and one developed diabetes mellitus. Ascending cholangitis occurred in half of the patients and several had multiple episodes. In those patients who had bile culture, *E coli* or *Klebsiella* were the offending organisms. Response to treatment with tetracycline, ampicillin or a cephalosporin was usually rapid.



### *Response to Treatment*

There have been four deaths. One patient died of renal failure and severe hepatic dysfunction four years after the initial diagnosis, one patient died of cirrhosis and ovarian carcinoma after ten years and another died of liver failure and portal hypertension after four years. The fourth patient, who had ulcerative colitis, developed a carcinoma of the colon which was successfully resected but died of an oat cell carcinoma of the lung four years after the diagnosis of sclerosing cholangitis.

The remaining eight patients are alive. Four are symptom-free, three have troublesome pruritus and one has a persistent biliary fistula. The period of follow-up ranges from 1-18 years, the average being 6.2 years.

### DISCUSSION

Primary sclerosing cholangitis is a disease, the aetiology of which is at present unknown. Various causes have been suggested, including bacterial or viral infection, damage by gallstones and chemical injury by deconjugated bile salts. However the relative sparing of the mucosa casts doubt on these aetiologies and the most accepted theory at present is a disorder of immunity.<sup>5</sup>

In common with other series the majority of our patients were male with a wide age range when first seen.<sup>9</sup> The usual presentation in the literature is obstructive jaundice,<sup>6, 8, 10</sup> but in our patients abdominal pain was a frequent initial symptom. The association between sclerosing cholangitis and ulcerative colitis has been widely recognised<sup>3, 6, 8, 11</sup> and sclerosing cholangitis is one of several forms of hepatic disorder that can occur with inflammatory bowel disease.<sup>12</sup> Recent data suggest that the prognosis of patients with ulcerative colitis and sclerosing cholangitis may not be as favourable as was originally thought.<sup>13</sup> An association has also been noted with Crohn's disease,<sup>14</sup> retroperitoneal fibrosis and Riedel's thyroiditis,<sup>15</sup> but none of our patients had any of these conditions. The ESR was usually increased but few other haematological disturbances were found in our patients though others have reported lymphocytosis and eosinophilia.<sup>7, 10, 15</sup> Biochemical analysis confirmed the obstructive nature of the jaundice with grossly elevated alkaline phosphatase levels being also a constant finding in other series.<sup>8, 9, 16</sup> In common with others we found immunological screening to be negative in our patients although occasionally weakly positive SMA, AMA and ANF have been reported.<sup>9, 11</sup> Immunological levels in sclerosing cholangitis are usually normal<sup>17</sup> though raised IgM has been reported.<sup>9</sup> Six of our patients had increased IgA; this finding has not previously been noted.

Routine liver biopsy provided only non-specific information and this has also been the experience of others. Attempts have been made to improve diagnostic accuracy by staining for copper deposits<sup>9</sup> but these also occur in the late stage of primary biliary cirrhosis.

Several reports have suggested that laparotomy is essential for accurate diagnosis<sup>11, 16</sup> but percutaneous transhepatic cholangiography using the Chiba needle is the investigation of choice<sup>5, 9</sup> and displays the beaded appearance of the bile ducts, decreased arborisation and bile duct strictures of varying length.<sup>18</sup> In sclerosing cholangitis proximal bile duct dilatation rarely occurs unlike traumatic strictures.<sup>7</sup> ERCP is also a useful adjunct to diagnosis but, in already obstructed ducts, there is some risk of precipitating acute cholangitis. Intravenous cholangiography was unhelpful.

Treatment of this rare condition is difficult to evaluate as there have been no controlled trials. Antibiotics have a definite role in treating bouts of ascending cholangitis and cholestyramine usually relieves pruritus. Most controversy surrounds the use of steroids. Schwartz and Dale considered steroids to be of benefit<sup>10</sup> and in 1973 Schwartz reported a satisfactory response in nine out of eleven cases.<sup>19</sup> Myers and his colleagues<sup>4</sup> noted reversal of abnormal radiological findings but others have observed only temporary remission.<sup>1, 6, 11, 16</sup> Very few encouraging results of treatment with azathioprine have been reported<sup>20</sup> and occasionally natural remission of the disease was thought to have occurred.<sup>14</sup> Our experience closely corresponds to that of Schwartz and a dose of 5-10 mg of prednisolone daily appears to keep the disease in remission for prolonged periods though careful monitoring is required to avoid steroid-induced side effects such as osteoporosis.

A variety of surgical procedures designed to decompress the biliary tree have been advocated and some reports have suggested that this is the only effective form of treatment.<sup>6, 11</sup> Prolonged T tube drainage until there is radiographic evidence of remission of the disease has been proposed.<sup>6, 7</sup> For patients with diffuse bile duct involvement either prolonged decompression using an external T tube or internal drainage with a T tube following hepaticojejunostomy<sup>1</sup> have been advised. Temporary transhepatic biliary drainage has also been used. For patients with localised strictures considerable benefit has been obtained from choledochoduodenostomy or choledochojejunostomy for distal strictures and hepaticojejunostomy with Roux-en-Y for proximal strictures. Our patients who required surgical by-pass have had encouraging results though the numbers are small. Recently Pitt and his colleagues have reported an aggressive surgical policy in which they carried out choledochenteric anastomoses in patients with a major area of extrahepatic blockage or primary involvement of the extrahepatic ducts. At a mean follow-up of 52 months after surgery thirteen out of seventeen patients were considered to have had a good result.<sup>21</sup>

Widely differing prognoses for this condition are given in the literature. Although Schwartz and Dale reported only one death in their six patients,<sup>10</sup> most authors conclude that the prognosis is poor.<sup>1, 5, 6</sup> Recently Thompson and his colleagues<sup>22</sup> have suggested that primary sclerosing cholangitis is a heterogenous disease with four subgroups each with differing prognoses, namely: (1) sclerosing cholangitis affecting primarily the distal common bile duct, (2) sclerosing cholangitis occurring soon after an attack of acute necrotising cholangitis, (3) chronic diffuse sclerosing cholangitis and (4) chronic diffuse sclerosing cholangitis associated with inflammatory bowel disease. Group 1 seemed to benefit from choledochenteric anastomosis and to do well. If the patients in Group 2 survived the initial acute attack, they also seemed to have a good outlook. Eight deaths occurred at a mean of 4.3 years among the 29 patients in Groups 3 and 4. However, there were eleven long-term survivors. In those patients with ulcerative colitis, colectomy appeared to confer no benefit on the biliary disease.

In this series eight of the twelve patients are still alive at mean follow-up of 6.2 years and there are six long-term survivors of more than five years. There were two deaths from liver failure and the other two patients died from ovarian carcinoma and oat cell carcinoma of the lung respectively. We consider that long-term

maintenance treatment with prednisolone combined with internal choledochenteric anastomosis for tight strictures, especially of the distal ducts, has proved satisfactory.

Ascending cholangitis requires prompt treatment with an appropriate antibiotic and close monitoring of the dose of steroids is needed in order to minimise side-effects. There may be a future role for dilatation of localised strictures under radiological screening and the place of endoscopic transnasal biliary drainage awaits evaluation.

### SUMMARY

The clinical features, investigation, treatment and prognosis of twelve patients with primary sclerosing cholangitis are presented. Ten patients were male. The initial symptom in eight was abdominal pain, sometimes recurrent, and jaundice developed in all but one of the twelve patients. A raised serum alkaline phosphatase level was the most consistent biochemical abnormality and percutaneous transhepatic cholangiography showed good evidence of the extent of the changes in the biliary tree. Eleven patients were treated with prednisolone and three underwent definitive surgery. Four deaths have occurred in the series; two from liver failure, one from an ovarian carcinoma and the other from a malignant lung tumour. Of the remaining eight patients, six have been alive for more than five years. All are receiving a small maintenance dose of prednisolone.

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# **ROUTINE MEASUREMENT OF HAEMOGLOBIN A<sub>1</sub> AT THE DIABETIC OUTPATIENT CLINIC**

by

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FOLLOWING the introduction of insulin therapy in 1922 one of the major problems in the long-term management of insulin-dependent diabetes was the lack of a convenient, reliable and objective test of longer term glycaemic control. In the 1960's and early 1970's haemoglobin A<sub>1</sub> (HbA<sub>1</sub>, glycosylated haemoglobin) was shown to be elevated, usually, in diabetic patients<sup>1-3</sup> and its biochemical structure was elucidated.<sup>4-6</sup> The mid-1970's saw many reports confirming that measurement of HbA<sub>1</sub> provided an accurate and objective assessment of glycaemic control in the preceding 6 to 8 weeks, a period corresponding to the approximate half-life of the average red blood cell. The vast majority of these studies were either cross-sectional in design<sup>7-10</sup> or, if longitudinal, carried out in the controlled atmosphere of the clinical research centre or hospital ward.<sup>11, 12</sup>

On the basis of this accumulated knowledge, measurement of HbA<sub>1</sub> has become commonplace in many diabetic outpatient clinics. The purpose of this communication is to report how accurate measurement of HbA<sub>1</sub> has been successfully introduced to a large diabetic outpatient clinic in such a way that the result is available at the time of the patient's routine clinic visit. In addition, we have tried to assess whether, in insulin-treated patients, the test yields information which is distinct from that already available from plasma glucose measurements.

## **ORGANISATION OF OUTPATIENT CLINIC AND BLOOD SAMPLING**

The diabetes clinics of the Royal Victoria Hospital, Belfast, are held on Tuesday and Friday mornings of every week and, once a month, also on a Saturday morning. Medical staff comprises at least two consultant physicians assisted by two junior grade doctors at each clinic. In addition, a "blood sampling" clinic is held every Wednesday morning, where patients, due to attend the following Friday, Saturday or Tuesday, have their blood samples drawn. This suits many of the patients who live not more than two or three miles from the hospital. Those patients who live further away arrange to have blood samples taken on the Monday or Tuesday either at home or at their local health clinic or general practice, and post them to the hospital laboratory. The custom has been for some years that patients who are solely on dietary therapy have fasting samples taken, while those on oral hypoglycaemic agents or insulin have samples taken 2.5 hours after breakfast.

This organisational scheme was already in existence before we introduced routine measurement of HbA<sub>1</sub> in December 1980. We surmised that the drawing of an extra 5 ml of blood and labelling of an extra specimen bottle would not place an intolerable strain on the system.

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## LABORATORY METHODS

Plasma glucose is measured by the neocuproine method. The blood samples are put into fluoride-containing bottles.

Samples for HbA<sub>1</sub> measurement are drawn into EDTA and stored at 4°C until Wednesday afternoon. Red cells are then incubated in normal saline at 37°C until Thursday morning, to remove any "unstable" glycosylated fraction.<sup>13-17</sup> Haemolysates are then prepared and HbA<sub>1</sub> is measured by agar gel electro-endosmosis<sup>18</sup> (Corning Medical Ltd, Halsted, Essex). The normal range in our laboratory is 3.7 to 7.2 per cent. Coefficient of variation within assay is 1.6 per cent and between assays 6.4 per cent. Two standard haemolysates (high and normal HbA<sub>1</sub>) are run each week to ensure that there is no "assay drift".

As we were concerned that postal handling or delay might affect HbA<sub>1</sub> results we obtained duplicate samples from 21 diabetic and 5 control subjects. These were assayed after being sent directly to the laboratory or through the post. Mean  $\pm$  SEM levels were similar —  $9.25 \pm 0.36$  per cent (direct) v.  $9.39 \pm 0.39$  per cent (postal), and the correlation between the two sets of samples was extremely close,  $r = 0.94$ .

During the period under investigation (December 1980 to February 1982) the laboratory were able to process approximately 110 samples for HbA<sub>1</sub> estimation each week and have them available, with the results on computer printout sheets, for the appropriate clinics. The maximum number of samples presented to the laboratory in any one week was 210, and these were processed satisfactorily in the normal way.

## ASSESSMENT OF HbA<sub>1</sub> AND COMPARISON WITH PLASMA GLUCOSE

We have retrospectively identified 302 insulin-treated patients who, from December 1st 1980 to February 28th 1981 (initial visit) had HbA<sub>1</sub> measured for the first time under the scheme outlined as part of the routine clinic visit. Table 1 gives details of the patient characteristics. These patients were reviewed either twice or three times more in the subsequent 9 to 12 months; 181 patients were reviewed at 2 to 4 months (first review), 194 at 5 to 7 months (second review) and 248 at 9 to 12 months (third review) after the initial visit. In every case there was a period of at least 2 months between successive reviews. HbA<sub>1</sub> and plasma glucose (2.5 hour post-breakfast) were recorded for each clinic attendance.

TABLE 1  
*Characteristics of 302 insulin-treated patients*

Male/Female	147/155
Duration of diabetes (years) — range	< 1 to 48
— median	12
Age (years) — range	7 to 83
— median	49

To attempt to compare the information available from each of these parameters in individual patients changes from the values at the initial visit, to subsequent reviews, were arbitrarily defined as follows:

**HbA<sub>1</sub>**

- increase of  $\geq 1.5$  per cent = clinically important increase
- decrease of  $\geq 1.5$  per cent = clinically important decrease
- increase or decrease of  $< 1.5$  per cent = no change

**Plasma glucose**

- increase of  $\geq 3$  mmol/l = clinically important increase
- decrease of  $\geq 3$  mmol/l = clinically important decrease
- increase or decrease of  $< 3$  mmol/l = no change

These arbitrary values were chosen to take into account the reproducibility of the assay methods and, in the case of plasma glucose, the likelihood of day-to-day fluctuation.

Analysis of HbA<sub>1</sub> and plasma glucose values showed that neither of these parameters was normally distributed within the population studied. Therefore, comparisons were made using the Wilcoxon signed rank test for matched pairs, and correlations using the Kendall rank correlation coefficient. The conventional level of significance ( $p < 0.05$ ) has been used in all analyses.

## RESULTS

Initial visit HbA<sub>1</sub> values ranged from 5.5 to 21.0 per cent, with a mean  $\pm$  standard error of  $10.7 \pm 0.13$  per cent. Plasma glucose ranged from 1.0 to 33.6 mmol/litre with a mean of  $10.16 \pm 0.35$  mmol/litre. There was a weak but statistically significant correlation between HbA<sub>1</sub> and plasma glucose — Kendall correlation coefficient = 0.18,  $p < 0.001$ . Similar weak correlations between HbA<sub>1</sub> and glucose were found at the first, second and third reviews, with Kendall correlation coefficients of 0.18, 0.21 and 0.12 respectively.

TABLE 2

*Comparison of HbA<sub>1</sub> and plasma glucose at the initial visit with values at reviews*

	<i>HbA<sub>1</sub> (per cent)</i>		<i>Glucose (mmol/l)</i>	
	<i>Initial</i>	<i>Review</i>	<i>Initial</i>	<i>Review</i>
First review (n = 181)	10.83 $\pm$ 0.17	9.94 $\pm$ 0.16*	10.49 $\pm$ 0.46	10.06 $\pm$ 0.50
Second review (n = 197)	10.70 $\pm$ 0.15	10.13 $\pm$ 0.16*	10.05 $\pm$ 0.42	10.41 $\pm$ 0.46
Third review (n = 248)	10.74 $\pm$ 0.14	10.74 $\pm$ 0.15	10.43 $\pm$ 0.38	10.55 $\pm$ 0.39

Results as mean  $\pm$  SEM.

\*  $p < 0.001$ , Wilcoxon signed rank test. All other differences are not statistically significant.

Comparisons of mean HbA<sub>1</sub> and plasma glucose at the review visits with the mean levels at the initial visit, on a paired basis, are shown in Table 2. The significant falls in mean HbA<sub>1</sub> seen in patients at the first and second reviews were not reflected by decreases in plasma glucose. At the third review neither of these parameters differed significantly from mean levels at the initial visit.

Table 3 indicates the number of patients who had an increase, decrease, or no change (as defined above) in HbA<sub>1</sub> and plasma glucose at the first review compared to the initial visit. Thus, of the 70 patients whose HbA<sub>1</sub> level decreased, plasma glucose decreased in only 25, was unchanged in 28, and increased in 17. It can be seen that the changes in the two parameters were concordant in only 74 of 181 patients (40.8 per cent).

TABLE 3  
*Comparison of individual "clinical changes" in HbA<sub>1</sub> and plasma glucose, from the initial visit to first review*

		<i>Plasma glucose</i>		
		<i>Decrease</i>	<i>No change</i>	<i>Increase</i>
HbA <sub>1</sub>	Decrease	25	28	17
	No change	28	42	26
	Increase	3	5	7

Similarly, when HbA<sub>1</sub> and plasma glucose at the second review were compared in this fashion to levels at the initial visit, the concordance between the tests was 84 out of 194 (43.3 per cent), and for the third review 98 out of 248 (39.5 per cent).

## DISCUSSION

Apart from accurate laboratory measurement of blood or plasma glucose, assay of HbA<sub>1</sub> is the only truly objective index of glycaemic control available to the practising diabetologist. Other aids to assessing control, such as urine sugar testing and home monitoring of blood glucose, are heavily dependent upon the patients' subjective interpretation and co-operation and are, in any case, less accurate.

Saunders et al demonstrated, in 1980, that measurement of HbA<sub>1</sub> by agar gel electroendosmosis could be performed while patients waited at the clinic.<sup>19</sup> However, their HbA<sub>1</sub> measurements, without prior incubation of red cells in saline, would have included the "unstable" Schiff base fraction which may be influenced by short term fluctuations in blood glucose.<sup>13, 17</sup> Like them, we chose to measure HbA<sub>1</sub> by agar gel electroendosmosis. This has proven to be an accurate, reproducible method, with many samples being processed easily by a single technician. The problem of "unstable" HbA<sub>1</sub> has been overcome by incubating samples overnight in saline. The apparent reliability of results from postal samples should enable our system to be adopted by many other clinics where an extra visit to the hospital for blood sampling is inconvenient or impractical. When, in December 1980, we started this scheme, we confined routine HbA<sub>1</sub> measurement to insulin-treated patients as we were unsure if the laboratory could cope with the workload. Approximately a year later we expanded to include all patients at the clinic and the laboratory now satisfactorily processes 180 to 200 samples each week.



In comparison to plasma glucose, measurement of HbA<sub>1c</sub> is relatively expensive; consumable materials alone cost 20 to 30 times more per test. We felt it important, therefore, to try to assess whether these two objective tests of glycaemic control give distinct information, if HbA<sub>1c</sub> is to be measured routinely in patients with a condition as common as diabetes. The retrospective analyses we have presented here show this to be the case.

First, reductions in mean HbA<sub>1c</sub> at the first and second reviews after the introduction of the test were not reflected by changes in the mean plasma glucose (Table 2). Secondly, the data concerning the *trend* of glycaemic control in individual patients shows that, according to the criteria we laid down, conclusions drawn from the two parameters would differ in approximately 60 per cent of cases (Table 3).

These conclusions are perhaps not unexpected bearing in mind that we are comparing HbA<sub>1c</sub> with single post-prandial plasma glucose measurements. We believe that similar conclusions would hold for fasting plasma glucose measurements in insulin-treated patients. No doubt a greater degree of agreement would be obtained from comparison of HbA<sub>1c</sub> with the mean of several plasma glucose levels, but we feel that our clinic is probably not unique in relying, in the majority of patients, on a single blood sample approximately every two to four months.

Conclusions concerning the possible impact which the availability of HbA<sub>1c</sub> measurement may have on glycaemic control should not be based on a retrospective analysis such as this. Nevertheless, speculation on why HbA<sub>1c</sub> levels decreased at the first and second reviews, but (disappointingly) increased again after 9 to 12 months, seems reasonable. It might be argued that since the number of patients at the first and second reviews was considerably less than at the initial visit, too much should not be read into the decreases in HbA<sub>1c</sub>. However, analysis showed no difference in terms of age, duration of diabetes or HbA<sub>1c</sub> and plasma glucose at initial visit, between attenders and non-attenders at the first and second reviews. In any case every patient was included in either the first or second review. It is probable, therefore, that there was indeed an initial improvement in glycaemic control in the cohort.

We would suggest two possible explanations for this initial but unsustained improvement. First, enthusiasm for a “new” test on the part of the medical personnel, with subsequent waning, could certainly account for the described phenomenon. Interestingly, similar unsustained improvements in diabetic control have been observed after the introduction of home blood sugar monitoring programmes.<sup>20-22</sup> A second possible explanation is that we were observing a seasonal variation in glycaemic control, quite unrelated to any specific therapeutic manoeuvre. Our study began in mid-to-late winter, with first and second reviews largely in spring and summer, and final reviews in autumn through winter. It is easy to believe that more intercurrent illnesses (e.g., viral) in winter and dietary excess over the festive season would contribute to poor control, whereas increased physical activity in the spring and summer would tend to have the opposite effect. Although a seasonal variation in the onset of clinical diabetes is recognised,<sup>23</sup> we are not aware of any previous reports of seasonal variations in glycaemic control in established diabetes.

It is rather disappointing that approximately one year after introducing HbA<sub>1</sub> measurement routinely at our clinic, we seem to have achieved no substantial improvement in glycaemic control in the majority of the 302 insulin-treated patients studied. However, we believe we have demonstrated that accurate HbA<sub>1</sub> measurement can be provided with little or no disruption to established clinic routine, and that this test yields clinically useful information not previously available.

## SUMMARY

Measurement of glycosylated haemoglobin (HbA<sub>1</sub>) by agar gel electroendosmosis was introduced as a routine test at a large teaching hospital diabetic outpatient clinic. An initial reduction in HbA<sub>1</sub> levels, in 302 insulin-treated patients, was not accompanied by a corresponding decrease in post-prandial plasma glucose levels, and was not sustained after 9 to 12 months. Changes in individual HbA<sub>1</sub> and plasma glucose were concordant in only approximately 40 per cent of observations. The facility of HbA<sub>1</sub> measurement appears to give clinically distinct information, but has not in itself led to an improvement in glycaemic control.

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# **A STUDY OF 100 CONSECUTIVE REFERRALS IN A UNIVERSITY PSYCHIATRIC CLINIC\***

by

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TO a psychiatrist working in a university student health centre, the factors affecting mental health and academic functioning of students is of interest for it is well known that rapid social change creates stresses detrimental to psychological stability. Accordingly a study was taken in the mid-seventies to look into the referrals to a psychiatric clinic in the Student Health Centre [now renamed as the University Health Centre (1983)] at the Queen's University of Belfast. Although the clinic had then been running since 1969, the mid-seventies were chosen because by that time, the student health physicians (the main source of referral) had become more adept at recognizing the cases which required more specialized psychiatric help. This was, no doubt, due to their own increased knowledge of psychological illness gained by the regular discussion groups with the particular psychiatrist involved. Although the main source of referral was through the student health doctor, some were also referred, firstly at the student's own request, secondly, through the faculty because it was recognized by the dean or tutors that the student's performance academically had suddenly deteriorated or that his/her behaviour was somewhat erratic, and thirdly, through friends or family of the student.

## **METHOD AND RESULTS**

Of the undergraduate population of the university as a whole, 93 per cent came from Northern Ireland, six per cent from the rest of the United Kingdom and one per cent from abroad. Less than 50 per cent of the students lived away from home.

This study concerns 100 consecutive referrals to the Student Health Centre Psychiatric Clinic during the period 1973-1975. They were all seen personally by the author. The students were attempting a primary degree and had attended the clinic voluntarily. The new referrals to the psychiatric clinic of the Student Health Centre during the period were distributed in each faculty as shown in Table I. These figures are compared with the percentage distribution of undergraduates in each faculty. There were three times as many males as females although males outnumbered females by 1.7 to 1 in the university as a whole.

Table II shows the diagnostic categories into which the ill students were classified. They were also broken down into those who graduated and those who did not. Twenty-eight per cent of those referred failed to graduate.

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\*Based on a paper read at the British Student Health Conference, April, 1982.

TABLE I

	<i>Patients referred for psychiatric opinion (Percentage)</i>			<i>Undergraduates in each Faculty (Percentage)</i>		
	<i>Male</i>	<i>Female</i>	<i>Total</i>	<i>Male</i>	<i>Female</i>	<i>Total</i>
Agriculture	3	0	3	2.5	0.5	3
Architecture	1	0	1	1.8	0.2	2
Arts	24	22	46	12	19	31
Dentistry	2	0	2	2	1	3
Economics	5	0	5	6	3	9
Engineering	5	0	5	9.8	0.2	10
Law	7	0	7	5	1	6
Medicine	8	2	10	11	5	16
Science	19	1	20	12	7	19
Theology	1	0	1	1	0	1
TOTAL	75	25	100	63.1	36.9	100

TABLE II

*Formal Psychiatric Illness*

	<i>Obtained Degree (Percentage)</i>		<i>Failed to get Degree (Percentage)</i>		<i>Total (Percentage)</i>
	<i>Male</i>	<i>Female</i>	<i>Male</i>	<i>Female</i>	
PSYCHOSES					
Schizophrenia	2	1	3	0	6
Manic depression	1	0	1	0	2
Endogenous depression	2	1	1	0	4
Epilepsy	1	0	0	0	1
NEUROSES					
Anxiety with/without phobias	17	7	3	1	28
Reactive depression	10	1	0	0	11
Obsessional neurosis	3	1	0	0	4
Anorexia nervosa	0	2	0	2	4
Hysteria	0	1	0	0	1
PERSONALITY DISORDER					
Inadequate and immature personality	7	4	11	3	25
Sex disorders	9	1	1	1	12
Drugs	1	0	1	0	2

The most common illnesses were the neurotic disorders which accounted for 48 per cent of the total with anxiety with or without phobias the most prominent. The general impression in most cases was that the anxiety had been reactive to either maturational or environmental stresses. The most common precipitating factors were problems of relationships with fellow students and tutors, difficulties in achieving mastery of the subject studied, separation from family or actual phobias about attending lectures or tutorials. Personality disorders and psychosis accounted for 39 per cent and 13 per cent respectively with men more conspicuous than women in these latter categories.

Students living away from home in university residences or in lodgings accounted for 62 per cent of the referrals and the most vulnerable academic years for students were their first and final years. All those who were seen were followed through their university career and as already stated, 28 per cent failed to finish their degree and left the university. Of those who failed to graduate, academic causes were responsible in 47 per cent, personal reasons in 32 per cent, health factors in 14 per cent and disciplinary action in seven per cent. When one looked at the differences between those who had been treated and went on to obtain their degree with those who failed to graduate, it was apparent that the latter showed a prominence of personality disorder in the form of immature personality or drug dependency and sexual problems compared to the successful group (60 per cent compared to 30 per cent).

TABLE III

<i>FACULTY</i>	<i>Number referred for psychiatric advice</i>	<i>Number failing to graduate</i>
Agriculture	3	1
Architecture	1	0
Arts	46	19
Dentistry	2	0
Economics	5	2
Engineering	5	1
Law	7	2
Medicine	10	0
Science	20	3
Theology	1	0
TOTAL	100	28

Table III shows the percentage of affected students who failed to graduate in the different faculties. It can be seen that in general the most vulnerable were those in the academic or theoretical disciplines while those in faculties with a strong vocational or practical attitude were more successful.

TABLE IV

	Number who graduated 72	Number who failed to graduate 28
Failed Eleven Plus or repeated 'A' Levels	11 (15%)	7 (25%)
Family history of psychiatric illness	28 (39%)	19 (68%)
A history of suicidal attempts	5 ( 7%)	2 ( 7%)
Living away from home	43 (60%)	18 (64%)

In Table IV a comparison is drawn between those who graduated and those who failed to graduate with respect to academic achievements before coming to university, a family history of psychiatric illness, a history of suicidal attempts and living in lodgings or university accommodation. Those failing to graduate had a slightly increased evidence of academic problems before entering university and a much greater family history of psychiatric illness.

An attempt was made to follow up the patients in this survey after they had left the university by posting out a short questionnaire to each patient and also by personal contact. There was unfortunately, only a 50 per cent response but the answers to the questions posed are presented in Table V.

TABLE V  
*Follow-up after leaving university*

	<i>Graduate group</i>	<i>Failed group</i>
Needing further psychiatric help after leaving	11 (15%)	22 (78%)
Able to obtain employment in United Kingdom	68 (95%)	18 (66%)
Felt university education helped them in obtaining employment	65 (90%)	6 (22%)

## DISCUSSION

University students are specially suitable for epidemiological study for a number of reasons. They are an important section of the population, both socially and medically. At university they are readily accessible for study and they form a discrete age group.

For some students academic success may have been achieved at the cost of social restriction and consequent immaturity in spite of the fact that Ryle assumed that those reaching university are to some degree positively selected for mental health.<sup>1</sup> The years of late adolescence are devoted by the student to learning at the same time as he is forming emotions and ideals into a practical life-style influenced and

affected by events in his personal, family and national-political existence. All of these form potential stresses which can add to or detract from his studies through their effect on his emotional and, therefore, on his intellectual functioning.<sup>2</sup> Several studies of adolescents have shown that adolescent turmoil is not the norm. We need not expect every young person to have pathological upsets, but also we must be wary of what we do label as illness.

Student identity problems and difficulties emotionally are at times quite frightening to him but one thing that is working in the student's favour is his youth. In general, students are resilient and responsive to new ideas and their approach to life is still fluid. They can adapt to change and what is more important, mature. What might appear as relatively severe problems in a later age group do not have the same poor prognosis during adolescence.<sup>3</sup>

The sex distribution of formal psychiatric illness in this study, namely more males than females, is in keeping with previous studies published, as is the higher incidence in first year entrants.<sup>4, 5, 6</sup> The difference in emotional stability between theoretical and practical students were discussed by Howell et al.<sup>7</sup> They stressed that a relevant factor may be that scientific students have a well defined career structure and prospects. Davy also made comment that the man who wants to be a doctor, lawyer or engineer has the ambition first and then makes the best use of his academic ability.<sup>8</sup> Experience in Belfast, however, would suggest that the entrants to the practical sciences and especially medicine are possibly better selected than those entering the other theoretical faculties. Academic achievement prior to entering university, that is Eleven Plus and 'A' Level results, did not appear to be of great importance, although in the group failing to graduate, problems with Eleven Plus examinations and 'A' Levels (Table IV) were slightly greater than in those who graduated.

The failure to graduate rate in this study of 28 per cent is much higher than the average for the whole university community (4.5 per cent).<sup>\*</sup> It should, however, be noted that only the more serious cases were seen and this is supported by the large constitutional element (68 per cent with a family history) in the group. Also this failure group, when followed up after leaving university, showed that 78 per cent required further psychiatric help later. A recent study in Southampton University<sup>9</sup> found similar results. It could be argued that as 60 per cent of those failing to graduate had a personality disorder they, as a consequence, made little effort to acquire knowledge at the university. Half of the academic failures presented themselves at the psychiatric clinic during the last term of the academic year and just before their June examinations. Nevertheless, two thirds of them were able to obtain employment in this country even though only a fifth felt their university career had helped them. The fact that all the medical and dental undergraduates referred eventually graduated is worth mentioning. This may be due to the support and close contact which these faculties provide for the students, especially in their clinical training.

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<sup>\*</sup> Students completing all or part of their final year are included as final year students. Students intending to graduate or graduating but who progressed to a further year's study are excluded.



This study highlights a number of factors which may help the university authorities to prevent psychiatric breakdowns in undergraduates or help those who are emotionally disturbed. Students in the theoretical faculties appear to be the most vulnerable group and may need greater surveillance and counselling in their first and perhaps final years.

The gap from home and school to the university setting is likely to be felt more by the student coming from a rural community and being accommodated in university halls and lodgings. More support therefore should be considered for this group of students. With the greater opportunities for young people nowadays to obtain a university career, a gap is developing between the student and his family. Therefore, some measures to retain contact with home and relatives should be developed. The student is a lonely figure who appears alone at the clinic.

Many students develop anxiety reactions simply because they do not know how to study and to differentiate between what is important and unimportant in their reading. They also have difficulty in developing a proper examination technique. The high incidence of neurotic disorders in this survey with problems of work, study and academic difficulties would suggest a closer link with student and academic staff should be encouraged. Psychological assessment at entry would help to identify those persons who may be in need. Since this study was completed a psychological questionnaire has been arranged for every undergraduate entering the university. This is filled in by the student when he attends for his routine medical examination. It will be of interest to see if this procedure can throw any light in helping to identify the more vulnerable group in the university.

The student often feels alone in the large university setting and is reluctant to acquaint himself with those who may be able to help him. Therefore closer liaison between all the disciplines in the university, for example counselling service, psychologist, doctors (in the Student Health Centre), administrative and academic staff, need to be developed with the student.

## SUMMARY

One hundred consecutive patients referred to a university psychiatric clinic over a two-year period have been studied. Students pursuing a course with a large practical element were less prone to psychiatric illness than those in a more theoretical field. Males outnumbered females by three to one. Students who came from a rural community and living in halls of residence or lodgings were also more vulnerable. Twenty-eight per cent of those referred did not graduate for academic, personal, health or disciplinary reasons. A follow up study was embarked upon and the results discussed. Neurotic illness with or without phobia was the most common disorder encountered. Recommendations are offered as a means of identifying and perhaps decreasing the incidence of psychiatric illness in students.

I am indebted to Mr. John McCloy, Manager of Data Processing Services, The Queen's University of Belfast for all his efforts in producing the necessary statistics and to Mrs. Diane Spratt and Mrs. Sharon Cherry for the secretarial work in its preparation.

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# **OUTCOME OF PREGNANCY IN A RUBELLA OUTBREAK IN NORTHERN IRELAND 1978-1979**

by

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IN Northern Ireland, during 1978-79, there was a major outbreak of rubella. A similar outbreak affected the rest of the United Kingdom and other countries throughout the world.<sup>1,2</sup> We have investigated the outcome of pregnancies of women who were diagnosed virologically as having rubella in the first four months of pregnancy during 1978-79. In addition, all infants born in 1978-79 and suspected of having intrauterine rubella infection, or who were conceived during 1979 and born during 1980, were tested and those who had rubella specific immunoglobulin M (IgM), were followed up.

## **MATERIALS AND METHODS**

Where possible acute and convalescent sera were obtained from pregnant women after contact with rubella. Rubella haemagglutination-inhibition (HI) antibody was titrated in sera after removal of inhibitors with dextran sulphate—CaCl<sub>2</sub>.<sup>3</sup> Trypsin modified human O erythrocytes were used.<sup>4</sup> Antibody titres were expressed as reciprocals. Rubella specific IgM was measured in sera by the indirect fluorescent antibody test on rubella infected VERO cells.<sup>5</sup> Sera were absorbed with monkey liver powder, heat aggregated human immunoglobulin to eliminate non-specific staining due to possible rheumatoid factor in serum<sup>6</sup> and protein A Sepharose (Pharmacia) to decrease interfering IgG.<sup>7</sup>

All infants, born in 1978, 1979, and the first 9 months of 1980, who were clinically suspected of having congenital rubella had their sera fractionated by ultra centrifugation on a sucrose density gradient<sup>8</sup> and fractions containing rubella specific IgM were detected by the indirect fluorescent antibody test as above.

In pregnant women after contact with rubella, acute rubella infection was diagnosed if the acute sera had no detectable antibody ( $< 10$ ) and a four-fold or greater rise of antibody developed in convalescent sera. In women who were bled later than one week after contact and who had high ( $\geq 160$ ) but not rising titres of rubella antibody, rubella specific IgM was measured and, if detected, indicated rubella virus infection within the previous two months.

The minimum immune titre of rubella HI antibody<sup>9</sup> in this laboratory is 20 which is equivalent to at least 15 International Units per ml. of rubella antibody.<sup>10</sup> Rubella HI antibody at a titre of 20 or higher, indicates that the pregnant woman is immune either in a routine screening test, or within one week after contact with rubella.

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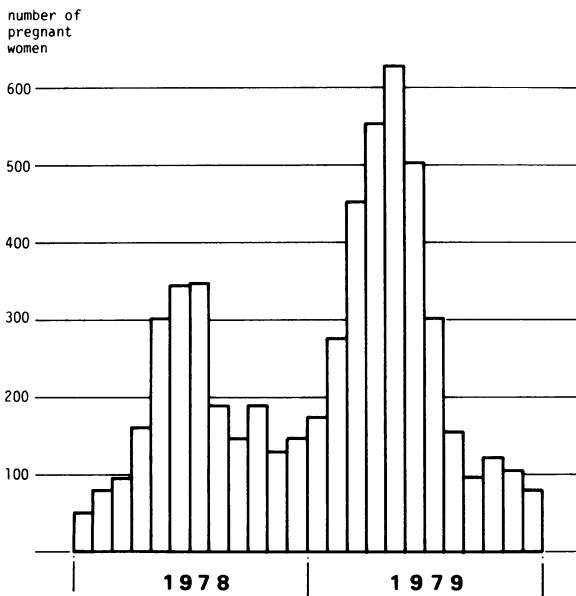
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## RESULTS

**Before the outbreak:-** Between June 1973 and October 1975, sera from 1000 pregnant women attending antenatal clinics in hospital or general practice throughout Northern Ireland were tested for rubella HI antibody; 81.2 per cent had a titre of 20 or greater, and were regarded as immune.

**The outbreak:-** The number of pregnant women who either had a rash or who were in contact with suspected rubella and whose blood was sent to the laboratory is shown in the Figure. The peak incidence was June and July during 1978, and May during 1979. Although the number of requests dropped during the winter of 1978-79, they did not fall below pre-outbreak levels. The commonest history of contact with rubella was with a young child in the same household. There were 1229 more requests for rubella serology in pregnant women in 1979 compared with 1978. Many other blood samples from pregnant women who did not have rubella or contact were received as a result of extensive coverage of the outbreak on the news media.



*Figure.*

*Rubella antibody requests per month from pregnant women in Northern Ireland who had a rash or contact\* with suspected rubella.*

\*Date of contact is shown and not date of request.

### *Rubella in Pregnant Women*

Sixty-seven women in 1978 were diagnosed by the laboratory as having had rubella. On follow-up, two were found not to be pregnant, and five could not be traced. Of the 60 remaining women, 31 had greater than four-fold rising titres of rubella antibody while 29 had raised but static rubella antibody titres with rubella specific IgM present in their sera. Thirty-two (53 per cent) women were recorded as having had a rash. In 1979, 108 women were diagnosed by the laboratory as having had rubella. On follow-up, 11 were found not to be pregnant, and seven could not be traced. Of the 90 women remaining, 36 had greater than four-fold rising titres of rubella antibody, while 54 had raised but static rubella antibody titres with rubella

specific IgM present in their sera. Thirty-eight women (42 per cent) were recorded as having had a rash. Of the 150 women with proven rubella, the ages ranged from 16 to 40 years with a mean of 27.1 years. Geographically, 100 of these women were located in urban areas: Belfast (33), South Antrim (32), Craigavon (17), North Down (16) and Londonderry City (2).

In 1979, a 29-year-old woman had clinical rubella during the first month of gestation of her third pregnancy. Rubella specific IgM was present in her serum taken three weeks later. A female infant was born with hepatosplenomegaly and multiple congenital abnormalities which included patent ductus arteriosus, deafness, cataract, microphthalmia, and retinopathy. Rubella specific IgM was present in her serum. The mother had received Cendehill rubella vaccine eight years previously.

### OUTCOME OF PREGNANCY

Table 1 shows the outcome of pregnancy. Of the 150 pregnant women with proven rubella, 69 (46 per cent) had a therapeutic abortion. Of the 81 mothers who continued their pregnancy there were 69 (85 per cent) normal liveborn infants, three apparently normal stillbirths, and nine (11 per cent) infants with congenital abnormalities. These infants were followed-up, and Table 2 details the abnormalities. All nine mothers had a history of a rash during the pregnancy. Six of the nine infants were female, and three weighed less than 2500 grams. In two infants rubella specific IgM was not detected, but the interval between their date of birth and the date of testing was 20 and 23 months, respectively. Both babies had rubella HI antibody titres of 20, while antibody titres of toxoplasma, herpes simplex virus, and cytomegalovirus were not significant. Since rubella HI antibody had persisted longer than six months after birth, they are included.

TABLE 1

#### *Outcome of Pregnancy in Women with Laboratory Proven Rubella*

<i>Year</i>	<i>Number of women with proven rubella</i>	<i>Outcome of pregnancy</i>			
		<i>Induced abortion</i>	<i>Normal livebirths</i>	<i>Normal stillbirths</i>	<i>Abnormal infants</i>
1978	67 <sup>1</sup> (60)	27	27	2	4
1979	108 <sup>2</sup> (90)	42	42	1	5
Total	175 (150)	69	69	3	9

In 1978 and 1979, 2140 and 3369 (total 5509) women were tested.

<sup>1</sup> In 1978 5 women could not be traced, and 2 women were found not to be pregnant.

<sup>2</sup> In 1979 7 women could not be traced, and 11 women were found not to be pregnant.

( ) = Number of pregnant women with proven rubella traced.

TABLE 2  
*Abnormal Infants born to Mothers with Laboratory Proven Rubella*

<i>MOTHER</i> <sup>1</sup>			<i>INFANT</i>
<i>Gestation (weeks)</i>	<i>Birth weight</i>	<i>Sex</i>	<i>Clinical features</i>
10	3365	F	Deafness
8	3175	M	Systolic murmur, hepatosplenomegaly, purpura.
8	2180	M	Deafness, systolic murmur.
8	1620	M	Fallots tetralogy, hepatosplenomegaly, osteitis.
14	3310	F <sup>2</sup>	Generalised erythematous rash; Click right hip.
4	2400	F	Deafness, cataract, microphthalmia, and retinopathy, patent ductus arteriosus, hepatosplenomegaly.
7	3340	F <sup>2</sup>	Large interior fontanelle, bronchiolitis.
7	3005	F	Chest infections.
6	3062	F	Right cataract.

<sup>1</sup> All 9 mothers had a history of rubella in pregnancy.

<sup>2</sup> Rubella specific IgM negative but rubella HI antibody present.

*Abnormal infants with rubella specific IgM born to mothers not tested during pregnancy*

A further nine infants with rubella specific IgM born to mothers not tested during pregnancy were identified from sera sent to the Regional Virus Laboratory because congenital rubella was suspected in the infant (Table 3). Of these mothers, three had no history of rubella during pregnancy, and of the other six mothers, five had had a rash during pregnancy. The remaining mother had been in contact with rubella and had received human immunoglobulin. The abnormalities in the nine infants are detailed in Table 3. Five of the 9 infants were female and 4 weighed less than 2500 grams.

*Congenital rubella infants*

A total of 91 infants were tested for rubella specific IgM either because they had been born to women with proven rubella during pregnancy, or because congenital rubella was suspected in the neonatal period. Eighteen infants had rubella specific IgM in their sera. Two of these infants born in the first five months of 1978 were excluded from the study since they were infected *in utero* before the rubella outbreak, and 2 affected infants who only had rubella HI antibody, 20 and 23 months after birth, were included. Of the 14 mothers who had a history of clinical rubella, one mother had a history in the first month of pregnancy, 9 in the second month, 3 in the third month, and 1 in the fourth month. Of the 18 infants with congenital rubella infection, at the time of follow-up, 7 had deafness, 7 had had a skin rash, 7 had congenital heart disease, 5 had hepatosplenomegaly, 4 had congenital cataract, 2 had osteitis, and one had microcephaly. Two infants presented only with chest infections and bronchiolitis. One infant with hypospadias and a bifid scrotum, had Klinefelter's syndrome (47,XXY). His mother had been in contact with rubella at 8 weeks gestation and had received human immunoglobulin.

TABLE 3  
*Abnormal Infants with Rubella specific IgM born to Mothers not tested during pregnancy*

MOTHER		INFANT		
<i>History of rubella (R) or rubella contact (C) and gestation Weeks R/C</i>		<i>Birth weight</i>	<i>Sex</i>	<i>Clinical features</i>
12	R	2860	M	Hepatomegaly, purpuric rash, anaemia.
6	R	1644	F	Deafness, multiple eye defects, patent ductus arteriosus, aortic stenosis, purpuric rash, wide fontanelle, growth retardation (post natal).
8	C*	2380	M	Hyposadias, bifid scrotum, Klinefelter's syndrome.
8	R	3410	M	Deafness, jaundice, rash, microcephaly, spastic quadriplegia, osteitis.
NR	NR	2070	F	Hepatomegaly, thrombocytopenic purpura.
—	—	2920	M	Systolic murmur, purpura, thrombocytopenia, croup.
6	R	2235	F	Post natal growth retardation.
12	R	2510	F	Deafness, systolic murmur.
NR	NR	2722	F	Deafness, cataract, and microphthalmia, delayed development.

NR = not recorded.

\* = human immunoglobulin given.

— = no known contact.

TABLE 4  
*Number and Prevalence Rate per 100,000 Livebirths of Infants with Congenital Rubella in Northern Ireland*

<i>Year</i>	<i>Number of Livebirths</i>	<i>Number of Congenital Rubella Infants</i>	<i>Rate per 100,000 Livebirths</i>
1977	25,437	1	3.9
1978	26,237	5*	19.1
1979	28,179	11	39.0
1980	28,568	4	14.0
1981	27,297	0	—

\* includes the two patients born 1978 but not included in study because infected before onset of epidemic.

Table 4 shows the prevalence rate per 100,000 livebirths in Northern Ireland from 1977 to 1981. Before the outbreak the rate was 3.9 and reached a peak of 39.0 in 1979; in the post-outbreak period the rate fell to 14.0 in 1980, and so far no case of congenital rubella born in 1981 has been identified.

## DISCUSSION

In Northern Ireland, with a population of 1.5 million, all diagnostic virology is carried out by the Regional Virus Laboratory, and the monitoring of birth defects is undertaken by the Northern Ireland Genetics Service. As both these services are responsible for the whole of Northern Ireland, this facilitated the study of the effects of rubella in pregnancy during the outbreak. The outbreak took place against a background of 81 per cent of pregnant women being immune. Epidemic rubella usually appears in late winter and spring, but in the Northern Ireland outbreak the peaks were in June-July in 1978 and in May 1979. The number of cases of congenital rubella was greater in 1979 than in 1978, a finding similar to Scotland, whereas in England and Wales the pattern was reversed, with more cases occurring in 1978 than in 1979.<sup>1, 2</sup> The pregnant women with proven rubella lived in the more densely populated eastern area with only two occurring in Londonderry in the north-west, the second largest city in Northern Ireland.

The follow-up of 150 pregnant women with laboratory proven rubella revealed that 69 (46 per cent) had had a therapeutic abortion; in England and Wales the figure was 54 per cent.<sup>11</sup> If therapeutic abortion had been unavailable, a further 7 or 8 congenital rubella babies might have been born.

Five problems became apparent during the investigation of the rubella outbreak. The first problem related to the extensive news media coverage during the epidemic. The laboratory was swamped with specimens from many pregnant women who did not have rubella or any contact with rubella, yet were anxious, following the inaccurate reports of the risk of having a congenital rubella baby. The second problem concerned the exposure of pregnant women to rubella. During the outbreak it was noted that the commonest history of exposure was with young children suffering from rubella in her own home or elsewhere. However, in the United Kingdom the policy is to immunise girls only between their 10th and 14th birthdays which is ineffective in preventing rubella in younger boys and girls. Rubella vaccine is also strongly recommended for non-pregnant women of child-bearing age who are seronegative but this policy has not been implemented.

The third problem of rubella infection was that some women and their doctors were unaware of the infection. In 1978 and in 1979, only 53 per cent and 42 per cent of the rubella infected pregnant women had a rash. Since rubella embryopathy can occur with sub-clinical rubella infection,<sup>12, 13</sup> laboratory tests are important in women with a history of contact with rubella but without clinical symptoms. The fourth problem was that previous rubella immunisation was not a guarantee of immunity in a pregnant woman as in one of our patients. Rubella vaccine does not produce 100% immunity in those immunised.<sup>14</sup> In addition, some of those immunised may produce only low rubella antibody titres which may disappear later. The Cendehill rubella vaccine induces a lower seroconversion rate,<sup>14</sup> lower serum antibody titres and less rubella specific serum and nasopharyngeal IgA than the



RA27/3 rubella vaccine. Re-infections also are more frequent after Cendehill rubella vaccine.<sup>15</sup>

The fifth problem, despite widespread publicity of the outbreak in both local and national news media, was that some pregnant women in contact with rubella and who also developed a rash, did not have laboratory investigations carried out (Table 3). One mother, after contact with rubella, was given human immunoglobulin which failed to prevent the infection of the fetus with rubella virus. Human immunoglobulin in normal dosage does not prevent rubella infection but may sometimes prevent the development of symptoms.<sup>16</sup>

In the 81 pregnant women with proven rubella who went to term, only nine (11 per cent) had abnormal babies. However, it is possible that some apparently normal infants at birth may develop "late onset" disease in infancy.<sup>17</sup> From several prospective studies, the overall percentage of infants with rubella defects following rubella in the first 4 months of pregnancy is 14.4 per cent.<sup>18</sup> In our study 14 (78 per cent) of the 18 mothers with congenital rubella infants, had a history of clinical rubella during the first four months of pregnancy. A rubella infection which produces clinical symptoms in the mother is more likely to be associated with rubella defects in the baby than rubella infection without symptoms.<sup>11, 13</sup>

In our study, rubella infection in the mother during the second month of pregnancy resulted in 10 out of 14 (71 per cent) congenital rubella infants. This finding agrees with the increased risk of defects at this gestation found by Dudgeon.<sup>18</sup>

Seven of the 18 congenital rubella babies had birth weights below 2500g. Intra-uterine and extrauterine growth retardation is a feature of congenital rubella infection.<sup>11, 19</sup> Among our rubella babies there was a high prevalence of deafness, skin rashes, hepatosplenomegaly, congenital heart defects and cataracts, whereas, osteitis, pulmonary infections and microcephaly were much less frequent. Two infants had chest infections which may represent rubella interstitial pneumonitis. One baby with Klinefelter's syndrome has hypospadias and a bifid scrotum. Hypospadias was previously described in a rubella baby.<sup>19</sup>

The fact that 89 per cent of babies born to mothers with proven rubella were apparently normal at birth raises interesting questions. The virulence of the strain of rubella virus in a particular epidemic may influence the number of fetuses infected *in utero* or the HLA antigens of the mother and fetus may determine susceptibility to infection with rubella virus.<sup>20</sup>

The prevalence of congenital rubella is difficult to determine because of incomplete reporting of documented or suspected cases, and because of the difficulty in diagnosis. A National Congenital Rubella Surveillance Programme for Great Britain, was established in May 1971.<sup>21</sup> Following a peak of 11.9/100,000 livebirths in 1973, there was a gradual decline to 2.9 in 1977. In 1978 and 1979 the respective prevalence rates were 7.0 and 9.7.<sup>22</sup> In Northern Ireland, the prevalence rates for 1978, 1979, and 1980, were 19.1, 39.0, and 14.0, respectively, with a pre- and post-epidemic prevalence of 3.9 and 0 in 1977 and 1981. As a result of the 1978 rubella epidemic in Chicago, 31 infants with congenital rubella were identified, giving a prevalence rate of 48.9 between July 1978 and June 1979.<sup>23</sup> During the same period in Northern Ireland, the prevalence rate was 32.6.

## SUMMARY

Prior to the 1978-79 rubella epidemic in Northern Ireland, 81 per cent of pregnant women were immune to rubella. There was more rubella in 1979 than in 1978. During the epidemic 150 women in the first four months of pregnancy had laboratory proven rubella and of these, 70 (47 per cent) had a recorded rash, 69 (46 per cent) had a therapeutic abortion, and of the 81 women remaining, 9 (11 per cent) had babies with congenital rubella.

A total of eighteen congenital rubella infants were identified; nine were born to mothers with proven rubella, and nine to the mothers who had no investigations. In 14 of the 18 (78 per cent) mothers, there was a history of clinical rubella. Ten mothers were infected with rubella in the second month of pregnancy.

One mother, who had received Cendehill rubella vaccine eight years previously, had clinical rubella during pregnancy and delivered a baby with multiple congenital abnormalities. Another mother received human immunoglobulin after rubella contact in pregnancy; her baby had hypospadias, bifid scrotum, and Klinefelter's syndrome.

The prevalence rate (per 100,000 livebirths) of congenital rubella infants in Northern Ireland, was 19.1, 39.0, and 14.0, for the years 1978, 1979, and 1980, compared with 3.9 in 1977. To date no case of congenital rubella has been identified in infants born in 1981.

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# UNSUSPECTED Q FEVER ENDOCARDITIS — A CASE REPORT

by

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Q fever endocarditis is usually characterized by a history of contact with animals or animal products, subsequent weight loss, pyrexia and night sweats. Clinical features almost invariably include valvular involvement, hepatosplenomegaly and haematuria.<sup>1</sup> We report a case of Q fever endocarditis in an elderly woman who, despite high titres of antibody, initially had no features apart from valvular involvement.

## CASE REPORT

A seventy year old woman presented with tiredness and dyspnoea. There was no history of weight loss, sweating, anorexia or rash. Clinical examination revealed the signs of aortic stenosis and incompetence; there was no pyrexia, tachycardia, anaemia or hepatosplenomegaly. Routine haematological studies were normal and there was no haematuria, but the ESR was 43 mm/hr, the IgG level was raised at 23.2 g/l and Q fever complement fixing antibody titres, checked routinely in this unit, were elevated (Phase 1—1,600, Phase 2—400). There was no history of direct contact with animals though the patient lived in an area where her house was fronted by a road frequently used by cattle lorries. Cardiac catheterization confirmed fairly severe calcific aortic stenosis with mild incompetence. Neither the left ventricular angiogram nor echocardiogram showed vegetations on the aortic valve. In the absence of clinical features of Q fever endocarditis, antibiotics were initially withheld and over the next two months she remained well with normal haematological screening apart from a few abnormal mononuclear cells in the blood films. However, both phase 1 and 2 Q fever antibody titres rose to 3,200 and the IgG level rose to 34.32 g/l. There was still no anaemia, pyrexia or hepatomegaly but the tip of the spleen became palpable and the aortic diastolic murmur more pronounced.

Rifampicin 600 mg daily and co-trimoxazole two tablets twice daily was started but the co-trimoxazole was discontinued after three weeks, because of a skin rash which resolved on cessation of this drug.

During the next three months the antibody titres and immunoglobulin level remained relatively unchanged but the haemoglobin fell from 12.8 to 10.9 g/dl. With the patient becoming increasingly dyspnoeic on effort and at rest aortic valve replacement was considered necessary.

At operation the aortic valve was bicuspid and heavily calcified with low grade inflammatory process at the insertion of the valve leaflets. A size 23 aortic St. Jude valve was sutured in place.

Guinea pig inoculation with a suspension of the homogenised aortic valve in buffered saline was carried out at the Special Pathogens Reference Laboratory at Porton Down. Blood samples from all four guinea pigs before inoculation and after

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22 days showed a rise in Q fever phase 2 antibody titre from  $< 10$  to  $> 640$ , confirming active infection.

Six months after valve replacement she was asymptomatic with no signs of cardiac failure or aortic incompetence and the spleen was not palpable. Both phase 1 and 2 Q fever antibody titres had fallen to 200. Tetracycline treatment, which had been commenced post-operatively, was continued.

## DISCUSSION

For twelve weeks our patient with aortic valve disease had high antibody titres to *Coxiella burnetii* without typical clinical features. Previous reports have usually stressed a history of exposure, though this may be limited to loose straw in the neighbourhood<sup>2</sup> as possibly in this case. All eight cases reported by Varma and his colleagues had a history of exposure, pyrexia, night sweats and enlargement of liver or spleen, or both organs.<sup>3</sup> In one patient with infection of a ventricular aneurysm there was an absence of symptoms and signs.<sup>4</sup>

In this case elevated and rising antibody titres in the presence of valve disease indicated active infection, despite absence of the usual features. Earlier antibiotic therapy may have prevented the necessity for surgical intervention though valve replacement would eventually have been required. Furthermore, since Q fever may be a surgical hazard we suggest that Q fever antibody titres should be estimated routinely before valve surgery is undertaken.

We wish to thank Professor D. I. H. Simpson and Dr. D. A. Rutter of the PHLS Special Pathogens Reference Laboratory at Porton Down, Salisbury for their help.

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# SCREENING FOR CERVICAL CANCER IN GENERAL PRACTICE

by

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THE benefit of regular screening for cervical cancer is now generally accepted. In the Scandinavian Countries and British Columbia where the majority of women have regular smear tests there has been a substantial reduction in mortality from cervical cancer.<sup>1, 2</sup> Furthermore, tumours are being detected at an earlier stage of development, while mortality is now largely confined to those who have never been screened. Unfortunately similar trends have not been found here (Table I).

TABLE I

*Patterns of referral by stage in cancer of the cervix, N. Ireland*

Stage	1953-60	1968-72	1977-81
I	17%	21%	21%
II	49%	46%	46%
III	19%	21%	17%
IV	14%	12%	13%
	Burrows and Lynch	D. Lowry	Mathewson and Lowry, W. S.

The Northern Ireland review group on screening for cervical cancer which reported in 1981,<sup>3</sup> recommended a more intensive screening programme with an eventual three fold increase in cervical cytology tests. They also stated that general practitioners were in the best position to identify those women requiring cervical cytology and recommended that general practitioners should be encouraged to take more cervical smears. This paper describes a programme for cervical screening in a group practice and outlines the need for the greater involvement of general practitioners in cervical cytology screening.

## METHOD

It was decided that each woman in the practice aged between twenty-five and sixty who was considered at risk should have a smear routinely every three years. All married women in this age group, unless they were pregnant or had had a hysterectomy, together with the single women who were known to have had contraceptive advice, were considered at risk. The patients were sent a letter giving them a definite appointment with a female doctor in the practice. This letter was signed by all the partners in the practice and contained a leaflet on the importance of cervical cytology. Those who did not respond to the first letter were sent a second

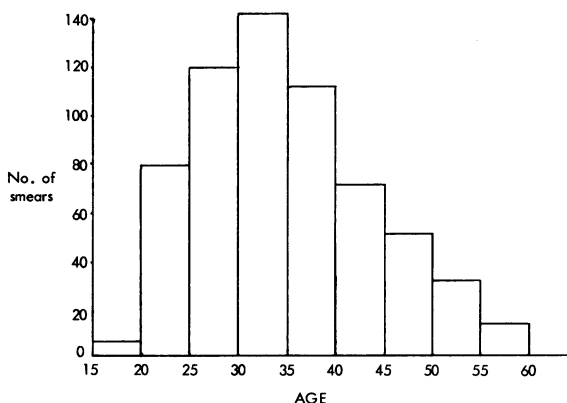
letter pointing out that more than four out of five women in the practice had by then had a smear within the past three years. The letter emphasised that it had been shown it was those who did not attend who were most at risk. Therefore, a further definite appointment was being offered.

As well as having a pap smear, each patient had a pelvic examination. Patients were recommended to carry out regular self examination of their breasts and were issued with an explanatory leaflet on breast self examination. Where time permitted patients were given anti-smoking advice and had their blood pressure recorded.

## RESULTS

In the practice of 8,100 patients there were 1527 women between 25-60 years. One hundred and sixty one were excluded because of pregnancy or hysterectomy, while 227 were single. Five hundred and ninety five patients (52 per cent) had a smear within three years. The age distribution of these women is shown in the Figure. Three quarters of these patients were under 40 years of age.

CERVICAL SMEARS PRIOR TO SURVEY , AGE OF PATIENTS



Five hundred and forty four other patients were sent for in groups of ten daily to four separate sessions per week over a six month period. Three hundred and sixty six attended 308 (56 per cent) on the first request and 58 (11 per cent) on the second request. At the conclusion of the survey 961 patients (84 per cent) of the patients at risk in this age group in the practice had a smear within the past three years.

There were two abnormal smears, only one of which was confirmed on repeat smear. This patient had a cone biopsy which histology confirmed as CIN Grade 11. The other patient is being kept under review. There were eighteen vaginal infections, all of which were treated. There were six patients with cervical polyps or cysts. There were sixty erosions ranging from small to large. The larger of these were treated in

TABLE II

<i>Abnormalities</i>	<i>No.</i>	<i>Rate/1000</i>
Erosions	60	164
Trichomonas	13	36
Monilia	5	14
Polyps, Cysts	6	16
Abnormal smears	2	5.5

the practice by the Cryoprobe. It is intended to report on the use of the Cryoprobe in general practice in a separate paper when its use has been fully evaluated. In this survey 40 per cent of the smears were eligible for payment under the general practitioners terms of service. The income derived was considerably greater than expenditure including secretarial time.

## DISCUSSION

This study has shown that if screening for cervical cancer only takes place at attendance for family planning advice, at postnatal examination, at hospital gynaecological outpatients and at the patient's request for a pap smear as happened prior to this survey in this practice, then this will result in the main in the screening of the younger age group, who are least at risk (see Figure).

These findings are in keeping with United Kingdom statistics where in 1977 there were 2.5 million smears examined, 57 per cent those under 35 years of age who had less than 15 per cent of the morbidity.<sup>4</sup> What is required is regular three yearly examination of all women from when they become sexually active until aged 60-65 years. With the benefit of an up-to-date practice age sex index the general practitioner is in a position to select and send for those requiring a cervical cytology test. As this and other studies show he is more likely than other agencies to get a good response from his patients. General practitioners have already increased their share of the number of cervical smears performed in Northern Ireland from 21 per cent in 1969 to 30 per cent in 1973,<sup>3</sup> but the regular screening of all those at risk would involve a considerably increased work load. This would involve ten smears per week for the first year for the average general practitioner to clear the back log and thereafter four smears per week. This does not seem a large task, but is a ten-fold increase on present work load. Unfortunately, only 22 per cent of general practitioners in Northern Ireland have up-to-date age and sex registers, which are essential for screening.<sup>5</sup> A central computer register of the computerization of general practice records would greatly facilitate this work. The one hundred and seventy eight women (16 per cent) still at risk in the practice who have not had a smear within the past three years have had a sticker put on their chart. It is our intention that they will be visited individually by our health visitor and will be counselled at their next surgery visit to have a cervical smear. It is our opinion that it is only in general practice that such a comprehensive programme of cervical screening can be achieved.

## SUMMARY

This paper shows that although half the women at risk in the practice had a smear within the past three years these were mostly young women, who were least at risk from cancer of the cervix. A screening programme which has resulted in 84 per cent of the women at risk in the practice having a smear within three years is described. This compares with 30 per cent coverage in the average practice.<sup>3</sup> A scheme to persuade the non-attenders is outlined. It is suggested that it is only in general practice that such a comprehensive programme of cervical screening can be achieved.

The authors wish to thank Dr J. H. Robertson and the Belfast City Laboratories for their co-operation and Mr R. Wallace for his helpful advice.



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# HIGH FREQUENCY JET VENTILATION AND ASPIRIN POISONING

by

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ASPIRIN poisoning is responsible for over 200 deaths per annum in England and Wales. Forced alkaline diuresis is advocated to hasten renal elimination of the drug when plasma salicylate levels exceed 500 mg/l, whilst charcoal haemoperfusion is the treatment of choice when plasma salicylate levels exceed 900 mg/kg.<sup>1</sup> This severity of poisoning causes gross respiratory, metabolic and coagulation disturbances, usually requiring cardiovascular and respiratory support.<sup>2</sup> Conventional low frequency, high volume ventilation is known to impair venous return and cardiac output, so that if respiratory support is needed this type of ventilation may further compromise the cardiovascular system.<sup>3, 4</sup> High frequency jet ventilation (HFJV) is an effective means of controlling ventilation without impairing cardiac output and was successfully used in this case to support respiration in a hypotensive patient suffering from aspirin poisoning.<sup>5</sup>

## CASE HISTORY

**Day 1:** A 55 year old man suffering from a depressive illness was admitted to Craigavon Area Hospital, having consumed 240 aspirin tablets (72g). He was sweating and unresponsive to verbal commands. Respirations were 46 per minute, blood pressure 150/100 mmHg and pulse rate 100 per minute. He had a marked respiratory alkalosis with compensatory metabolic acidosis — Table (line a). Blood was taken for salicylate levels and a stomach washout carried out. A forced alkaline diuresis was commenced using 8.5l of crystalloid fluid intravenously over 24 hours. 100 ml of this was 8.4 per cent sodium bicarbonate. Despite the use of diuretics

TABLE  
*High Frequency Jet Ventilation*

	<i>pH</i>	<i>PaCO<sub>2</sub></i>	<i>PaO<sub>2</sub></i>	<i>Base Deficit</i>
(a)	7.406	2.44	13.03	10.2
(b)	7.385	2.87	12.21	9.0
(c)	7.11	7.41	15.87	11.5
(d)	7.45	3.92	18.53	1.4
(e)	7.27	5.57	26.40	7.0
(f)	7.35	5.53	9.47	1.8
(g)	7.38	5.23	10.67	1.0

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pulmonary oedema occurred so a venesection was carried out, 600 ml of blood being drawn. At this stage the initial plasma salicylate level became available, it was 940 mg/l. The patient was therefore transferred to this hospital for charcoal haemoperfusion. Just prior to transfer, the patient became aggressive and was given chlorpromazine 50 mg intramuscularly.

**Day 2:** On arrival at the Royal Victoria Hospital, Respiratory Intensive Care Unit he was unresponsive to verbal commands and tachypnoeic (60 breaths per minute). Blood pressure was 90/65 mmHg and pulse rate 120 per minute. Widespread fine crepitations were heard on auscultation of the chest and chest x-ray was consistent with pulmonary oedema. However, blood gas analysis showed a well compensated respiratory alkalosis — Table (line b). Arterial and central venous pressure (CVP) lines were established in addition to electrocardiograph and urinary output monitoring. Ventilation was with a tidal volume of 800 ml 16 times per minute but this resulted in the blood pressure falling from 90/65 to 60/40 mmHg, with heart rate 120 per minute and CVP + 8 cm H<sub>2</sub>O. Transfusion with 80 g of human albumin and a dopamine infusion (40 µg/kg) only increased the blood pressure to 66/48 mmHg and respiratory acidosis developed due to inadequate ventilation — Table (line c). Since increasing the tidal volume would have a further deleterious effect on cardiac performance, HFJV was commenced via a Mallinckrodt Hi Lo Jet endotracheal tube using an Acutronic MK800 high frequency jet ventilator. This was set to deliver 100 breaths per minute at a driving pressure of 1.2 bar at FiO<sub>2</sub> 0.6. The blood pressure rose and heart rate fell. The dopamine infusion was reduced and a further blood gas analysis was satisfactory — Table (line d). HFJV was continued over the next 15 hours with a 5 minute period of 20 breaths per minute each hour, to prevent airway closure.

The right femoral vein and artery were cannulated in turn, the patient heparinized (2000 units heparin) and haemoperfusion started. Monitoring of coagulation, salicylate levels, electrolytes and blood gases were carried out regularly. Shortly after starting haemoperfusion platelets were transfused. In all, three charcoal columns were used during haemoperfusion, each for about three hours. Twelve hours after commencing haemoperfusion the patient was conscious, blood pressure 80/50 mmHg (dopamine 10 µg/kg/min), pulse 100 per minute, CVP 13 cm H<sub>2</sub>O and urinary output 100 ml/hour. Salicylate levels had now fallen to 239 mg/l and blood gas analysis was satisfactory — Table (line e).

**Day 3:** Weaning from the ventilator was commenced by gradually increasing the frequency of HFJV. Subsequently the patient was able to breathe on a T-piece and blood gas analysis was satisfactory — Table (line f).

**Day 4:** The patient was now awake and coughing so the endotracheal tube was removed and oxygen administered by face mask — Table (line g). Blood pressure was 120/60 mmHg and pulse 84 per minute. The patient's condition continued to improve over the next two days after which he was transferred to the referring hospital.

## COMMENT

During forced alkaline diuresis there is a risk of electrolyte imbalance and fluid overload. Pulmonary oedema may occur due to increased pulmonary vascular permeability as a result of the poisoning but is more frequently due to fluid overload. For these reasons central venous pressure monitoring is mandatory in addition to regular serum electrolyte and blood gas estimations.

Should pulmonary oedema occur forced alkaline diuresis should be discontinued and the oedema controlled with either diuretics or venesection. Since these methods failed to alleviate the pulmonary oedema in this patient, intravenous colloids and controlled ventilation were used. In this case the blood pressure fell during controlled ventilation and a respiratory acidosis occurred. HFJV was used in this case since it was considered a rapid means of reducing the  $\text{PaCO}_2$  without further compromising cardiac output. HFJV does not significantly alter the cardiac output or mean arterial blood pressure, yet arterial  $\text{CO}_2$  levels can be rapidly reduced by this means of ventilation. Since mean airway and intrathoracic pressure are not increased, venous return to the heart is not impaired. Conventional low frequency, high volume ventilation is known to impair venous return and cardiac output, due to the rise in intrathoracic pressure. In this case the patient was able to eliminate a considerable amount of  $\text{CO}_2$  during spontaneous breathing, yet with conventional IPPV (800 mg at 16 times per minute) ventilation was inadequate. During HFJV the small volume (80 ml) delivered close to the carina at 100 times per minute were very efficient at lowering the  $\text{PaCO}_2$  without impeding cardiac output. However, the use of small volumes over prolonged periods causes airway closure with resulting atelectasis. This was overcome by delivering larger volumes at slower rates for five minutes per hour. Weaning can be facilitated by increasing respiratory rate which results in a smaller tidal volume, allowing  $\text{PaCO}_2$  to rise.

## SUMMARY

A severe case of aspirin poisoning required charcoal haemoperfusion. A forced alkaline diuresis was attempted but led to fluid overload which did not respond to diuretic therapy. The patient subsequently became hypotensive and developed pulmonary oedema. Attempted control of respiration with conventional low frequency, high volume ventilation caused a further fall in blood pressure, despite inotropic support.

A respiratory acidosis also developed, so high frequency jet ventilation was substituted. The blood pressure rose and the respiratory acidosis rapidly disappeared. It was then safe for charcoal haemoperfusion to proceed.

The patient recovered over the following four days. We believe that the use of high frequency jet ventilation had a major role in the management of this patient.

We wish to thank Professor J. W. Dundee for his help and encouragement, also Mrs. S. Roy and Mrs. A. Quinn for typing this report.

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# RECTOVAGINAL FISTULAE FOLLOWING RADIATION TREATMENT FOR CERVICAL CARCINOMA

by

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DESPITE advances in radiation technology it is still not possible to prevent serious gastrointestinal or genitourinary complications after radiotherapy. The reported incidence of gastrointestinal complications following pelvic irradiation ranges from two to 17 per cent.<sup>1, 2, 3</sup> Although rectovaginal fistulae account for less than two per cent of these complications,<sup>4</sup> they may present a particularly difficult surgical problem from a diagnostic and therapeutic point of view. Five consecutive patients are described to illustrate some of the problems associated with their initial assessment and management.

## CASE REPORTS

Between October 1981 and March 1982, five patients with previously treated squamous carcinoma of the cervix were admitted with rectovaginal fistulae. A brief summary of these patients is given in the Table. The external radiation was given in fractionated doses (20 exposures) over four weeks and the intra-cavity radium dose was given over a period of 60 hours in all cases. The total radiation dose ranged from 8020 to 8420 rads. Two patients (Cases 1 and 3) also had an abdominal hysterectomy and bilateral salpingo-oophorectomy, two and one month after irradiation respectively.

TABLE

*Summary of five cases of rectovaginal fistulae*

<i>Case</i>	<i>Age</i>	<i>Stage</i>	<i>Time Interval XRT to Fistula</i>	<i>Type of Colostomy</i>	<i>Outcome and Duration</i>
1	31	II	8 months	divided trans loop	Well, 13 months
2	46	IIB	11 months	tranverse loop	Died, 2 months
3	44	IB	6 months	divided trans loop	Died, 2 months
4	55	IIB	11 months	tranverse loop	Died, 3 months
5	64	IIA	18 months	sigmoid end (Hartmann op)	Well, 8 months

Age: at time of diagnosis of Ca cervix.

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The original presentation of Case 1 was unusual in that the patient was pregnant at the time of diagnosis. A Caesarian section was carried out at 32 weeks and because the tumour was bleeding heavily; external radiation was started immediately. Examination under anaesthesia after four weeks revealed no extension of the disease into the parametrium. It was felt retrospectively that she had a Stage II lesion.

The average time interval between completion of radiotherapy and the development of the fistula was 10.8 months (range 6-18 months). Four of the fistulae occurred between 8 and 10 cm from the anal verge and the fifth (Case 5) developed 3 cm from the anus.

Recurrent tumour was present in patients 2 and 3. In Case 2 biopsies from the cervix and the edge of rectovaginal fistula both showed recurrent squamous carcinoma, although at the time of examination under anaesthesia the surgeon believed that no tumour was present. Case 3 showed no evidence of recurrent tumour in biopsies from the rectovaginal fistula but two months later when a large vesico-vaginal fistula developed, tumour nodules could be palpated on the pelvic side walls.

All five patients were treated with colostomies. Two had transverse loop colostomies fashioned over a skin bridge. A further two had divided transverse colostomies, with separation of proximal and distal colonic stoma. The fifth patient had a sigmoid end colostomy fashioned in the left iliac fossa with closure of the rectal stump.

Three patients died within three months of formation of their colostomy (Case 2, 3 and 4). Case 2 developed a malignant vesico-vaginal fistula one month after colostomy formation. An intravenous urogram showed only minimal function of the left kidney with a mass invading the left side of the bladder which was confirmed at cystoscopy to be necrotic recurrent tumour. This patient died four weeks later. Case 3 developed a vesico-vaginal fistula and acute renal failure two months after her colostomy formation. Ultrasound scan revealed marked dilatation of the pelvicalyceal system but at cystoscopy no recognisable bladder could be visualised. Tumour nodules could be easily palpated at the side walls of the pelvis. No further treatment was undertaken and the patient died six days later. This woman had also been troubled with prolapse of the colostomy. Case 4 was admitted to another hospital ten weeks after colostomy formation. She was bleeding per vaginam, and responded initially to blood transfusion but rapidly deteriorated two weeks after admission and died. Post-mortem examination was not carried out.

Cases 1 and 5 have remained well since their colostomies were fashioned. Both patients pass some mucus per rectum and per vaginam occasionally.

## DISCUSSION

The discomfort and distress associated with the uncontrolled discharge of flatus and faeces per vaginam in a woman with a post-irradiation rectovaginal fistula demands urgent treatment. Most authors recommend an initial colostomy because it is easier for the patient to manage than the fistula.<sup>5, 6</sup> The type and siting of the colostomy are important and depend on whether residual or recurrent tumour is present. This is sometimes difficult to determine with certainty because radiation fibrosis and necrosis can closely simulate carcinoma. We believe, however, that this

is vital to the initial management of these unfortunate patients so that the most appropriate colostomy can be fashioned. In Case 2 the surgeon carrying out the initial assessment felt at examination that no tumour was present. Routine paraffin sectioning, however, showed recurrent invasive squamous carcinoma. In retrospect it would have been more appropriate to have fashioned an end sigmoid colostomy. Intravenous urography and cystoscopy at the time of initial assessment of this patient might have shown the vesical extension of the tumour, which became apparent one month later.

Prior to the establishment of a colostomy in these patients we believe that full assessment including intravenous urography, cystoscopy, sigmoidoscopy and vaginal examination under anaesthesia with frozen section biopsy should be undertaken, involving surgeon, gynaecologist and not infrequently the urologist. If recurrent or residual tumour is found an end sigmoid colostomy with closure of the distal stump seems the most appropriate form of initial treatment. The permanent end colostomy in the left iliac fossa is easiest for the patient to manage, the motions are formed and colostomy prolapse is less likely to occur than with a transverse colon colostomy.

When the patient is found to be free of tumour then a colostomy fashioned in the proximal transverse colon is needed in the majority of cases. The function of this colostomy is to reduce the contamination caused by faecal bacteria and to eliminate the physical trauma of the passage of faeces. Defunction using a simple loop colostomy may be incomplete because of the proximity of the two stomas and we believe that in the peculiar situation of radiation damaged bowel, defunction must be complete. A modified Devine (divided transverse loop) colostomy with a skin bridge separating the two stomas will completely defunction the distal colon and rectum.<sup>7</sup> Irradiation damage usually extends well beyond the visibly damaged area and when the fistula is large and low in the rectum, an end sigmoid colostomy, as was used in Case 5 in the present series, may be the most appropriate initial treatment. Faecal diversion does not always prevent progression of radionecrosis and the surgeon may have to undertake further surgical intervention earlier than the recommended 9-12 months after colostomy formation.<sup>8</sup>

## SUMMARY

Five patients with rectovaginal fistulae following radiation treatment for carcinoma of the cervix are presented. Before the initial colostomy is fashioned it is vital to determine whether residual or recurrent tumour is present as this has a direct bearing on where the colostomy is sited. In the presence of tumour an end sigmoid colostomy is the most appropriate while in the absence of tumour a divided proximal transverse colostomy should be undertaken in the majority.



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# **PRELIMINARY REPORT — SPORTS INJURY CLINIC**

by

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IN the past 30 years there has been an increasingly scientific approach to sporting activities of all types, and athletes and their advisers have begun to ask for a number of specialist services. With this in mind it was decided to open a sports injury clinic, initially as a pilot scheme, in the accident and emergency department of the Belfast City Hospital. All acute or serious sporting injuries referred to this hospital are treated in the accident and emergency department in the first instance, but this clinic was started with the main objective of following up these acute injuries more closely and treating the more chronic injuries. Through the goodwill of other departments particularly physiotherapy, the clinic provides the facilities and expertise to deal with these problems. This paper reviews the work carried out by the clinic during its first 2½ years.

## **PATIENTS AND METHODS**

The clinic takes place on Monday afternoons in the accident and emergency department. In one session I see all the new patients including some acute injuries from the weekend. A second session is devoted to reviews and consultation with the physiotherapist. Initially the clinic was "open to all" but soon, due to rapidly increasing numbers, this immediate facility had to be curtailed and a referral system adopted. Patients are now referred by either their general practitioners, the university student health centre, or coaches.

Investigations, apart from radiographs, have been minimal, and the clinic has not placed an unreasonable burden upon supporting services. Treatment provided consists of physiotherapy, supportive measures, drugs and advice. Close liaison is maintained with the physiotherapist who may treat a proportion of the patients, after clinical assessment, on the day of their initial visit and then continue on a regular out-patient basis. The physiotherapeutic techniques available include ultrasound, infra-red, faradism, massage, friction, weight training, supervised exercise, stretch/mobilisation, and general advice on training. Supportive treatment consists of wool and crêpe bandages, plaster of Paris, tubular supports and various conventional splints. The drugs mainly used are analgesics and anti-inflammatory agents. Local steroid injections are given when necessary.

## **RESULTS**

A total of 1058 patients have been seen during the first 2½ years. There were 885 males and 173 females and the average age was 25 years. 64 were athletes of excellence (international standard). The anatomical classification of the injuries is shown in Table I. Two-thirds of the injuries involved the lower limb, 30 per cent knee, 19 per cent ankle, 16 per cent lower leg and calf, 5 per cent foot.

TABLE I  
*Distribution of injuries by anatomical site*

	<i>Number of injuries</i>	<i>Percentage</i>
Neck	12	1.1
Spine	68	6.4
Thorax and Abdomen	4	0.4
Shoulder	51	4.8
Arm and Elbow	20	2.9
Wrist and Hand	90	7.6
Thigh and Groin	63	5.9
Knee	320	30.2
Leg and Calf	173	16.4
Ankle	203	19.2
Foot	54	5.1
TOTAL	1058	100

The pathological causes of the injuries are shown in Table II. Of these the vast majority were soft tissue injuries, only 3.5 per cent being fractures and 1.2 per cent dislocations or subluxations. Ligamentous injuries were responsible for 34 per cent and injuries to muscle or tendon occurred in 31 per cent of patients.

TABLE II  
*Distribution of injuries by pathological cause*

	<i>Number of injuries</i>	<i>Percentage</i>
Ligament (strain etc)	360	34
Muscle and tendon (acute strain, chronic strain, rupture)	327	31
Miscellaneous soft tissue (contusion, haematoma, fascial compartment syndrome)	175	16.5
Miscellaneous joint (meniscus, capsulitis, synovitis, patella chondromalacia)	111	10.5
Fracture	37	3.5
Stress fracture	35	3.3
Dislocation/subluxation	13	1.2
TOTAL	1058	100

The sports responsible for the injuries are listed in Table III. More than half occurred in runners and footballers.

TABLE III  
*Distribution of injuries according to sport*

	<i>Number of injuries</i>	<i>Percentage</i>
Running	450	43
Football	302	28
Rugby	113	11
Athletics	84	8
Racquet games	29	2.6
Basketball/volleyball	25	2.4
Martial arts	15	1.4
Hockey/hurley/camogie	17	1.6
Swimming/diving	5	4
Ballet/gymnastics	6	5
Weight lifting	5	5
Water ski-ing	1	1
Golf	3	2
Horse riding	3	3
TOTAL	1058	100

83 patients were referred for specialists orthopaedic opinion, 26 requiring surgery and 57 resolving with conservative therapy. By far the commonest problem requiring referral was the injured knee (39 patients), the majority having symptoms suggestive of a torn meniscus or collateral ligament damage. Six patients had torn cruciate ligaments in association with meniscus or collateral ligament injury. One patient required pinning for osteochondritis dessicans. There were five cases of persistent back ache, two in weight lifters and three in long distance runners; two of these had symptoms and clinical findings consistent with nerve root compression which settled following a period of spinal traction.

One rugby player and one badminton player were found to have un-united fractures of the scaphoid when they presented at the clinic. Neither had sought medical advice at the time of the injury several weeks earlier, but eventually did so because of the persistent pain and weakness of the wrist. One healed satisfactorily following 18 weeks in plaster of Paris, the other is as yet only partially united after 16 weeks immobilisation and may require surgery. The two golfers with persistent wrist pain had de Quervain's tenosynovitis and responded to steroid injection. One hockey player required internal fixation with insertion of a K wire for an unstable fracture involving the proximal interphalangeal joint of the left index finger. Three patients sustained injuries to the thumb on the dry ski slope at Craigavon. One had complete rupture of the ulnar collateral ligament, requiring repair, one had an unstable fracture of the base of the first metacarpal requiring pinning and the third suffered a severe sprain which was simply strapped.

One patient ruptured his right achilles tendon while playing golf on a Sunday afternoon and was referred for assessment by his general practitioner the following Monday. He was admitted that evening for surgical repair. One somewhat unusual cause of severe forefoot pain in a middle distance runner, was found at exploration to be due to a digital neuroma — this is known as Morton's Toe. Following excision of the neuroma he made an excellent recovery. The various surgical procedures carried out are shown in Table IV.

TABLE IV  
*Surgical procedures*

Arthroscopy	15
Ligamentous repair of knee	5
Repair of Achilles tendon	1
Repair of ulnar collateral ligament of thumb	1
Internal fixation of fracture	2
Tibial compartment syndrome release	1
Removal of digital neuroma	1
TOTAL	26

## DISCUSSION

Trauma is the major component of the work of any large accident and emergency department, and professional or recreational sporting activity is the cause of a sizeable proportion of the injuries seen. The incidence and nature of these sporting injuries and the demands that they put upon the resources of the National Health Service were examined by Sleet and Dornan<sup>1</sup> at Southampton General Hospital. They found that sporting injuries produced more attendances than road traffic accidents in males in the 10-34 age group, and this would also be my experience in Belfast. They estimated that about 500 patients a year could be referred to their sports medicine clinic which would compare with the number of patients seen at the Belfast City Hospital sports injury clinic. Kirby<sup>2</sup> has discussed whether it is necessary to run a sports injury service separate from the normal hospital accident and emergency services. Speryn and Williams<sup>3</sup> confirm that prompt treatment, after medical referral, of any sporting soft tissue injury, will facilitate not only return to the sport but also to work. While most of the injuries could be managed with existing facilities in health centres and hospital accident and emergency departments, effective resolution in many cases demands a particular understanding by the clinician of sport-specific biomechanics and physio-pathology. Stanexu<sup>4</sup> has pointed out that special interest and experience is required if such injuries are to receive the particular care and attention they need. There is also the need to make available specialist facilities within 48 hours of the acute trauma, and this is not always readily available in some existing out-patient hospital facilities.

## SUMMARY

Between March 1981 and September 1983, 1058 patients were seen at the sports injury clinic. Runners and footballers accounted for over half of the attendances. Most of the injuries (92 per cent) were soft tissue and over two-thirds (70 per cent) involved the lower limb. 83 patients were referred for specialist orthopaedic opinion and 26 of these required operative surgery.

There is a place for a sports medicine clinic within a general hospital, with benefit to the athlete and to the general public. This clinic provides a valuable clinical and social need, involves interesting and satisfactory work for the medical personnel involved and does not divert medical, investigative or therapeutic services from what others may consider more important and deserving cases.

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# **CAREER PREFERENCE ENQUIRY AMONG QUEEN'S UNIVERSITY MEDICAL UNDERGRADUATES AND GRADUATES: STAGE III\***

by

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IN an attempt to obtain a better understanding of the factors which influence career decisions and stability of choice, Northern Ireland Council for Postgraduate Medical Education, in conjunction with the Faculty of Medicine at Queen's University, undertook a longitudinal survey of career preferences and desired location of practice of three cohorts of Queen's medical undergraduates in 1977. Questionnaires were distributed in the first instance to all second, fourth and final year students (Egerton, 1979) and in 1979 all those who had participated in the first stage were contacted again (Egerton, 1983). In 1981 all the 1979 respondents were contacted in this, the third stage.

## **METHOD**

Questionnaires were distributed to 131 final year students, 113 1979 graduates and 103 1977 graduates eliciting a response of 125 from the students and 113 and 88 respectively from the doctors. Individual replies were matched with questionnaires returned in the first two stages and changes noted.

## **RESULTS**

Apart from background information common to both, students and qualified doctors are dealt with separately in this section.

The mean ages of the three groups were 24, 26 and 28 and approximately one-third in each group was female. Predictably, the proportion of married respondents increased in accordance with age and income: 12 per cent in final year, 46 per cent among 1979 graduates and 64.8 per cent among 1977 graduates. One hundred and fifteen of the students, 106 of the 1979 graduates and 86 of the 1977 graduates were natives of Northern Ireland.

## **GRADUATES**

*Postgraduate Qualifications.* Seventy of the 1977 graduates had obtained at least one postgraduate qualification and in some cases three, four years after graduating. Ten had obtained Primary FRCS; 2 Final FRCS; 4 Primary FFARCS; 1 Final FFARCS; 6 Primary FRCR; 23 MRCP Part I; 12 MRCP Part II; 4 MRCOG Part I; 2 MRCP Path Part I; 4 MRCPsych Part I; 3 MRCGP; 18 DRCOG; 8 DCH and 1 DLD. There is little difference in the figures for men and women in this group: 84.2 per cent of the single men, 76.3 per cent of the married men, 90.9 per cent of the single women and 75 per cent of the married women had obtained at least one postgraduate qualification. The average numbers of qualifications, based on those who had obtained one or more were as follows: single men 1.3; married men 1.5; single women 1.5 and married women 1.4.

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\*This paper is a summary of a fuller report prepared for the DHSS (NI), copies of which are available on request from Northern Ireland Council.

Thirty of the 1979 graduates had obtained a postgraduate qualification two years after graduating; no-one had more than one. One had obtained an MD; 6 Primary FRCS; 4 Primary FFARCS; 7 MRCP Part I; 11 DRCOG; and 1 DCH. Just over 23 per cent of the single men, 41.2 per cent of the married men: 20 per cent of the single women and 15.8 per cent of the married women had a postgraduate qualification.

***Present Employment among Qualified Doctors.*** Eighty-one of the 1977 graduates were working full-time, three (women) were not working and four (women also) were working part-time. One hundred and seven graduates were working full-time, two women were on maternity leave, two women were not working and one man and one woman were working part-time.

Those who were working in both cohorts were asked to indicate the type of work they were doing (or their main employment, if engaged in more than one field), the grade of their present post, whether they intended to practice this field ultimately, and if not, which other areas of medicine they were considering. In both groups, general practice had attracted the greatest number (a total of 24.5 per cent) and medicine the next greatest (a total of 21.9 per cent). Among the 1977 group, radiology/radiotherapy was third with 10.5 per cent, and in the 1979 group, surgery was third with 10.8 per cent. Of the 1977 group 56.5 per cent were in registrar posts and 18.8 per cent were general practice trainees. Seventy-three per cent of the 1977 group were in SHO posts and 18 per cent were general practice trainees; 64.7 per cent were working in the same specialty as two years previously and 78.8 per cent intended to continue in the same specialty. Of the 1979 group 36.9 per cent were working in the specialty they had chosen two years previously and 55.9 per cent intended to continue in the same specialty. Two-thirds of the 67 doctors in the two groups who wished to change to another specialty or who were still undecided were considering general practice. A comparison of the results from the 1977, 1979 and 1981 studies shows that 34.1 per cent of the 1977 graduates and 17.1 per cent of the 1979 graduates were consistent in all three stages. The only specialties where respondents showed any degree of consistency were general practice, medicine and surgery in that order.

***Present Location of Qualified Doctors.*** Of the 192 graduates originating from Northern Ireland 171 were resident in the province at the time of completing the questionnaire. Sixteen were in Great Britain or the Republic of Ireland, two in Europe, one in Africa and two in unspecified countries abroad.

***Factors Influencing Decision to Leave the Province.*** Those who were living outside Northern Ireland were asked to indicate on a given list factors which influenced their decision to leave. Where a respondent has given more than one reason, he is counted more than once in the Table. Reasons listed under "others" are as follows. Five wished to broaden their experience both professionally and personally. Two left to join general practice vocational training schemes in England and Scotland because there were no posts available here. Three were in the Armed Forces and one left because of the political violence.

***Ultimate Location of Practice.*** Of the 171 Northern Ireland-born graduates who were resident here, 67.3 per cent planned to remain in the province in the long term;



TABLE  
*Factors influencing decision to leave the province*

	<i>1977 + 1979 Graduates</i>
Return to own country	5
Professional advancement	4
Better working facilities	1
Greater financial rewards	0
To obtain specialist experience with view to returning	3
Greater job satisfaction	1
Marriage or family reasons	6
Other reasons	11

15.2 per cent said they intended to leave, and the remainder had no strong feelings. Comparison of these figures with those of the previous studies showed that there was little change in either group between 1979 and 1981, after fairly dramatic increases in those wishing to stay here between 1977 and 1979. This stabilization is probably related more to the world job market than any other single factor. Certainly the turbulent political situation in Ulster has not been quoted as a major reason for emigration in any of the three studies conducted on Queen's graduates between 1977 and the present day. None of the 21 Northern Ireland-born graduates living outside the province had definite plans to return. One said he probably would, 11 said they might possibly, and the remainder said a definite no in answer to this question.

### **UNDERGRADUATES**

***Students' Current Career Preferences.*** Twenty-three of the 125 students claimed to have decided definitely on the broad field of medicine in which they wished to make their career. Another 87 were interested in a particular field but were still undecided; 13 had as yet no strong preferences but had decided against certain fields and two were completely undecided. Students who had decided on, or were interested in, a particular field, were asked to list in order of preference three broad areas of medical practice from a given list of six. General practice grew considerably in popularity between fourth and final year, attracting almost as much interest in 1981 as clinical hospital work with continuing responsibility (defined as medicine, the surgical specialties, obstetrics and gynaecology, paediatrics and psychiatry). The first two stages of this survey indicated that 25 per cent of the 1977 final year chose general practice and 50 per cent clinical hospital work with continuing responsibility; 30 per cent of the final year chose general practice and 40 per cent clinical hospital work with continuing responsibility. The distribution of preferences appears then to be changing steadily in favour of general practice, with little interest existing in areas other than these two, even as second preference. A few were willing to consider clinical hospital work with continuing responsibility (used in a broad sense to refer to radiology, anaesthetics and laboratory medicine) and community medicine as third choices but the majority did not state a third preference.

Those who had indicated a preference for a broad area of practice were then invited to specify three specialties in order of preference from a given list. The most notable points were the increased interest in general practice between 1979 and 1981 and the drop in popularity of surgery. On this occasion as in previous surveys there was a comparative lack of interest in anything outside general practice, medicine and surgery. The distribution of preferences of the 1981 final year students is similar to that of the 1979 final year: general practice 38.4 per cent in 1981 and 31.2 per cent in 1979; medicine 17.6 per cent in 1981 and 15.3 per cent in 1979; and surgery 8 per cent in 1981 and 9.9 per cent in 1979. Interest in specialties other than these three dropped from 27.4 per cent among the 1979 final year to 20.8 per cent among the 1981 final year. It was found in the second stage of the study that the preferences of the cohort at present under review had changed between second year (1977) and 1979 (fourth year) to form a pattern similar to that of the 1977 fourth year students. The further change between 1979 and 1981, forming a pattern similar to that of the 1979 final year students appears to reinforce the hypothesis suggested in the last report: that undergraduate career preferences may conform to a pattern, determined presumably by the emphasis given on the curriculum to the various specialties from year to year and by the influence of teachers.

Of the respondents 21.6 per cent were consistent between 1979 and 1981, (13 in general practice, 7 in medicine, 5 in surgery, 1 in ophthalmology and 1 in surgery). Only 7.2 per cent were consistent in all three stages of the survey (4 in general practice, 3 in surgery and 2 in medicine). Respondents were next asked to indicate specialties they had decided against. As with the final year students of 1979 it was the surgical specialties which fell most from favour, surgery, ophthalmology and otorhinolaryngology being discounted by an additional 22 to 25 per cent.

***Intended Location of Practice.*** The number of final year Northern Ireland-born students intending to stay here has risen from 47.8 per cent in 1979 to 65.2 per cent in 1981. The number wishing to leave has dropped from 18.3 per cent in 1979 to 10.4 per cent in 1981. The first two stages of this survey showed that the number of final year students intending to emigrate fell also between 1977 and 1979. The increasing difficulty in entering North America, traditionally the most favoured destination after Great Britain, probably accounts, in part, for this trend. Of the 1981 final year students wishing to leave, 6 wanted to go to Great Britain, 3 to Australia/New Zealand, 1 to Canada, 1 to the United States and 1 to India. Twenty-eight had no strong feelings about long-term location of practice.

## DISCUSSION

A tabulation of all three groups under review and the percentage remaining stable at each point in the survey, 1977, 1979 and 1981, shows that, in every case except one stability of specialty choice increases predictably with maturity and in relation to work experience. The one irregularity is the decrease in 1981 for the final year students. This lapse in stability is undoubtedly explicable in terms of the recent uncertainty among the student population about the job situation. Comments on the questionnaires suggest that the prevailing attitude is now to keep an open mind until one sees what is available.

Comparable with this study is one of the series of longitudinal surveys which have been conducted in Great Britain by Professor Parkhouse and his colleagues

(Parkhouse et al 1981). Five years after graduation, 62.5 per cent of the Parkhouse subjects had definitely made up their minds about specializing compared with 78.8 per cent of our 1977 graduates, four years after graduation. In the Parkhouse group 41.1 per cent had changed their intentions between 1975 and 1979 compared with 35.3 per cent of our group over a four-year period. Our figures concerning ultimate place of practice are less reassuring: 3.1 per cent of the Parkhouse group intended to emigrate and another 3.2 per cent said they probably would, in comparison with 14 per cent of our group who planned to leave.

The pattern of responses in this study confirms the trend suggested by the first stages. It would appear that, in the undergraduate years, specialty preferences are influenced by the time and emphasis allocated to particular subjects on the curriculum and possibly also by the enthusiasms and prejudices of the teachers. Attitudes towards the various specialties are clearly open to influence during this period and it seems likely that the specialties receiving more time and emphasis assume more prestige in the students' eyes. However, personal inclination is being modified increasingly among students and graduates by career opportunities. This is the final stage of the study to look at all three groups. It is planned in 1983 to concentrate on the 1977 graduates, examining more closely six years after graduation the reasons for their choice of specialty.

### SUMMARY

Questionnaires were distributed in 1981 to selected final year students and doctors who graduated in 1977 and 1979 in the third leg of a longitudinal career preference enquiry at Queen's University medical school. Replies were obtained from 95.4 per cent of the undergraduates and from 86.3 per cent and 85.4 per cent respectively of the qualified doctors. Seven per cent of the undergraduates, 17 per cent of the 1979 graduates and 34 per cent of the 1977 graduates were consistent in choice of specialty in all three stages. Eighty-eight per cent of the graduates were resident here at the time of completing the questionnaire and 60 per cent intended to practice here ultimately, the same proportions exactly as in 1979.

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## BOOK REVIEWS

**A RADIOLOGICAL INVESTIGATION IN RHEUMATOLOGY.** Edited by DM Forrester and JC Brown. Clinics in Rheumatic Disease, Vol 19, No 2. (Pp vii + 289-488. £11.75). London: Saunders, 1983.

IT is a great pleasure to be able unreservedly to recommend any book—and this is one of those occasions. To the physician or rheumatologist this small volume outlines precisely what can be expected from the various modes of imaging on patients suffering from bone or joint disease. To the radiologist it presents clearly the requirements of the clinician.

The chapters are well chosen. The illustrations are of excellent quality. A good balance is struck between conventional and more modern techniques, and it is of interest that the authors included computed tomography, ultrasound and nuclear magnetic resonance.

I strongly recommend this book to any clinician who is in the habit of writing X-ray requests for skeletal imaging, and to all radiologists who have to report on such requests. EMMcl

**IMMUNOLOGICAL INTERVENTION IN MEDICINE.** Edited by JF Mowbray. Clinics in Immunology and Allergy, Vol 3, No 2. (Pp vii + 205-361, Illustrated. £11.75). London: Saunders, 1983.

THE Editor states in his foreword that “in the sixties and early seventies enormous gains were made in our knowledge of basic immunological mechanisms, and that unfortunately, clinical use of this scientific foundation has been slow to appear.”

The book with nine short chapters, written by different specialists, presents the scientific background of various methods of treatment employed to alter immunological mechanisms, together with practical applications of each method. The balance between these two aspects is good, and all authors give fair comments of the shortcomings of treatment methods together with suggestions for future research and development. Immunological treatments other than standard immunosuppression used for many years, are discussed, and these include marrow and thymus replacement in the repair of immunodeficiency, the clinical use of cyclosporin A, the clinical use of transfer factor and the management of infection in the immunocompromised host.

Recently much interest has been shown in illness associated with altered immunoregulation, and this book will undoubtedly assist doctors in the management of patients with these illnesses. MH

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**EXOTICA.** By William StClair Symmers. (Pp xiv + 226. Illustrated. £8.95). London: Oxford University Press, 1984.

BILL Symmers, who recently retired from the Chair of Pathology at Charing Cross Hospital, is a distinguished graduate of this medical school, and a son of a former professor of pathology here. He has achieved world-wide fame as the editor and as a large contributor to *Systemic Pathology* published in multiple volumes over the last decade. That work is the major single reference source in the English language on problems in systemic pathology. In these days of more and more specialised monographs it is a unique and brilliantly co-ordinated presentation of the whole science.

As well as the widely based approach displayed in the textbook, Symmers has always cultivated an interest in entities rarely seen or rarely recognised and in unusual manifestations of disease. These are further histories similar to those recorded in his *Curiosa* (reviewed — *This Journal* 1974; 43: 177). Some may think these interesting accounts are described in detail more suited to an earlier and less hurried age, others may admire the circumlocutions before the outcome is revealed.

It is interesting to note that the book was produced as 'camera-ready copy' for the printers by the author on his Olivetti ET 221 electronic typewriter. Produced by conventional methods the cost would have prevented publication. The text and lay-out bear comparison with all but the best conventional print.

JEM

**OVARIAN CANCER.** Edited by PJ DiSaia. Clinics in Obstetrics and Gynaecology, Vol 10, No 2. (Pp vii + 153-368. Illustrated. £11.75). London: Saunders, 1983.

OVARIAN cancer now kills more women than any other genital tract malignancy. This book seeks to address itself to such a depressing picture and offers help with the problem. Contributors are all North American and provide a wide-ranging discussion on all aspects of the disease.

The opening chapter deals with pathology and emphasises the concept of low malignant potential in ovarian tumours. Attempts at early diagnosis have always bedevilled the clinician and chapters on immunology and tumour markers in relation to ovarian cancer reflect the continued efforts to establish an early diagnosis. As in all solid tumours accurate staging of the disease is of paramount importance and this is fully evaluated. The place of laparoscopy and second-look surgical procedures are critically assessed in the management protocol. Several chapters are devoted to the treatment of ovarian cancer and surgery remains the corner-stone — this is fully discussed. The place of immunotherapy and its potential is highlighted but at present has limited clinical application. Two chapters discuss radiation therapy; this treatment enjoyed popularity in the seventies but has since lost favour in many institutions. The attractive concept of radioisotope therapy within the abdomen is evaluated but results appear to be disappointing. Adjuvant chemotherapy provides the main thrust in treatment schedules. Chapters are devoted to chemotherapeutic experience of three large American referral centres. It is always difficult to interpret clinical trials with various agents and a strong temptation exists to identify a successful combination of drugs if a few patients respond favourably. Such eyeball statistics are not acceptable in the centres of excellence! The problem of clinical trials in ovarian chemotherapy are considerable and varied opinions from these institutions highlight the difficulties. The final chapter is devoted to germ-cell tumours—a rare but important clinical entity and present-day treatment is fully evaluated.

This book confirms the healthy state of gynaecological oncology in the USA demonstrating the increased sophistication and need for referral centres. It is a detailed book requiring careful reading for all who have a special interest in the subject. It is not suitable for light reading at bedtime and indeed may be of little interest to the perinatologist! It is to be highly recommended to those interested in ovarian cancer.

EBB

**PREPARATION FOR MRCP, Part II.** Edited by Paul Siklos and Stephen Olczach. (£9.95). Lancaster: MTP Press, 1983.

THIS book brings together a series of articles first published monthly in the Hospital Update Journal. I enjoyed the monthly contest consisting of multiple choice questions and case histories which were practical, not contrived and which were illustrated or amplified by excellent photographs and X-ray reproductions. The collected material now provides an excellent introduction to the prospective candidate and will make him familiar with the format of the examination. Equally useful is the information and advice on how to prepare for the clinical part of the examination and there is also an excellent section on aids for X-ray interpretation. I can recommend it not only to those candidates for the MRCP but also to those long past examinations who wish to measure their skills against those of their junior colleagues.

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OVARIAN cancer now kills more women than any other genital tract malignancy. This book seeks to address itself to such a depressing picture and offers help with the problem. Contributors are all North American and provide a wide-ranging discussion on all aspects of the disease.

The opening chapter deals with pathology and emphasises the concept of low malignant potential in ovarian tumours. Attempts at early diagnosis have always bedevilled the clinician and chapters on immunology and tumour markers in relation to ovarian cancer reflect the continued efforts to establish an early diagnosis. As in all solid tumours accurate staging of the disease is of paramount importance and this is fully evaluated. The place of laparoscopy and second-look surgical procedures are critically assessed in the management protocol. Several chapters are devoted to the treatment of ovarian cancer and surgery remains the corner-stone — this is fully discussed. The place of immunotherapy and its potential is highlighted but at present has limited clinical application. Two chapters discuss radiation therapy; this treatment enjoyed popularity in the seventies but has since lost favour in many institutions. The attractive concept of radioisotope therapy within the abdomen is evaluated but results appear to be disappointing. Adjuvant chemotherapy provides the main thrust in treatment schedules. Chapters are devoted to chemotherapeutic experience of three large American referral centres. It is always difficult to interpret clinical trials with various agents and a strong temptation exists to identify a successful combination of drugs if a few patients respond favourably. Such eyeball statistics are not acceptable in the centres of excellence! The problem of clinical trials in ovarian chemotherapy are considerable and varied opinions from these institutions highlight the difficulties. The final chapter is devoted to germ-cell tumours—a rare but important clinical entity and present-day treatment is fully evaluated.

This book confirms the healthy state of gynaecological oncology in the USA demonstrating the increased sophistication and need for referral centres. It is a detailed book requiring careful reading for all who have a special interest in the subject. It is not suitable for light reading at bedtime and indeed may be of little interest to the perinatologist! It is to be highly recommended to those interested in ovarian cancer.

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The treatment of germ cell tumours is one of the most rapidly advancing fields in clinical oncology and current developments in this area are comprehensively discussed. Precise staging of these lesions is essential prior to treatment and the chapter on Imaging is one of the best sections in the book. Again monitoring the progress of germ cell tumours often depends on the presence of tumour markers and reference is made to the importance of these in several chapters. The volume is somewhat expensive but the glossy format presumably accounts for this. It is an important new book in this field. WSL

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The next chapter deals with the relationship between FTS (facteur thymique serique, recently renamed thymulin) and T cell activation, in particular the growth of interleukin-2 producing T cells. Then follows a chapter on the effects of various thymic hormones on human lymphocytes *in vitro*, a chapter on the structure and biology of the thymosin peptides and a chapter dealing with similar aspects of thymulin. The book concludes with a chapter on the evaluation of some thymic hormone levels in serum with respect to age and diseases and two chapters on therapeutic adventures with thymic hormones mainly in various immunodeficiency states.

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