Volume 54, No. 2. OCTOBER 1985



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# THE ULSTER MEDICAL JOURNAL

*Published on behalf of*

*THE ULSTER MEDICAL SOCIETY*

ISSN 0041-6193

*The Ulster Medical Journal, Volume 54, No. 2, October 1985.*

# The Ulster Medical Journal

# 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 at the beginning of the paper.

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# The Ulster Medical Journal

VOLUME 54

PUBLISHED BY
THE ULSTER MEDICAL SOCIETY
1985

## CONTENTS

***Acknowledgements***

The Ulster Medical Journal acknowledges the generous contributions from the following bodies, without which it would not be possible to continue publication:-

Royal Victoria Hospital Medical Staff Committee, Royal Group of Hospitals Free Funds, Belfast City Hospital Free Funds, Ulster Hospital Dundonald Medical Staff Committee, Queen's University Belfast Grant from Senate Funds and the Northern Ireland Council for Postgraduate Medical Education.

*The Ulster Medical Journal, Volume 54, No. 2, October 1985.*

# THE ULSTER MEDICAL SOCIETY

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This covers one volume (two numbers) of the Journal.

*The Ulster Medical Journal, Volume 54, No. 2, pp. 89 – 108, October 1985.*

# The distinctiveness of Belfast medicine and its Medical School

An address given to the Ulster Medical Society, 16 May 1985.

Peter Froggatt

## PROLOGUE

On 8 October 1835, exactly 150 years ago, the 'Board of the Faculty of the Medical Department' of the Royal Belfast Academical Institution (hereinafter Inst) met for the first time — the first faculty board meeting of the first medical school in Ireland outside Dublin. Five 'professors' constituted the Board — John L. Drummond MD (anatomy and physiology, and botany), Thomas Andrews MD (chemistry), J.D. Marshall MD (materia media and pharmacy), Robert Little MD (midwifery and diseases of women and children), and John McDonnell (surgery). They had much in common: sharing an Ulster commercial, professional or farming background they shared also a confidence in the enterprise though prudently tempered with the hope that the persistence which had sustained their ambitions through the disappointments of the past two decades had been worthwhile and that a healthy and virile child had now been born which under their care would grow to robust manhood. Today's Faculty of Medicine at Queen's is the direct descendant of that precarious yet optimistic board: optimistic, in the almost arrogant confidence of its members; precarious, in that in four short years it lost John McDonnell and his successor (Surgeon Ferrar), saw Robert Little quit Belfast under a cloud albeit a feathery one, and gained only three (out of an optimistically proposed twelve) new members, one being a replacement — Robert Coffey MD (surgery), William Mateer MD (botany, from the overburdened Drummond), and Henry MacCormac MD (theory and practice of physic).

The Board stamped on the school from its very beginning certain distinctive features which microcosmed the circumstances and structure of the broader Ulster society which spawned and succoured it, and these can be traced to the present day. It seems appropriate that, on the Faculty's sesquicentennial anniversary, certain fundamentals of its foundation and development should be recalled and its distinctive features identified.

Many distinguished predecessors and colleagues too numerous to list have written of our medical school, its institutions and its personalities, and in recent years I have been privileged to join them.[1-7] This paper intends to complement, not rival nor duplicate, those that have gone before. Being mainly synoptic it must eschew much detail; readers seeking fuller accounts are referred to the more specialist sources, some of which are listed in the bibliography.

As primarily a university man, I may have presented interpretations which some readers will consider too favourable to the college at the expense of the hospital role and perceptions. Correctives abound in the exemplary and familiar works of Strain, Allison, Fraser, Craig, Calwell, Marshall, Hunter and Simms, among others.

Sir Peter Froggatt, MA, MD, LLD (Hon), DSc (Hon), PhD, DPH, FRCP, FFCM, FRCPI, FFCMI, FFOMI, MRIA, Vice-Chancellor, the Queen's University of Belfast.

## THE FIRST PERIOD: 1835-1849

### *Foundation*

Our medical school developed earlier than those of Cork, Galway, and what is now University College Dublin, and for two main reasons: the rapid industrialisation and accompanying dynamic growth of Belfast — 13,000 in 1782 became some 50,000 in 1831 and incredibly some 100,000 in 1851; and the religion of the majority of its citizens (Presbyterianism). Presbyterians, though a bare overall majority, dominated commercial life — only four of the 60 or so founder members of the Belfast Chamber of Commerce in 1784 were of other persuasions.[8] Outside Belfast they constituted an extensive reticulum of rural tenants, agrarian suppliers, general tradesmen, small independent farmers, and an important because literate smattering of doctors, notaries and clergy. They wished their sons to 'improve' themselves beyond field and counting-house but were denied many traditional avenues of patronage: medicine, the law, and the church were the 'professional' exceptions. Access to college education however was limited. Maynooth was (mainly) a Catholic theological seminary. Trinity College Dublin and Oxbridge disadvantaged them. The Scottish universities and the Royal College of Surgeons in Ireland (hereinafter RCSI) did not. Dublin — the natural choice as the metropolis — was culturally and geographically remote, expensive, and considered morally dangerous. Most therefore chose Glasgow or Edinburgh — no closer, cheaper, or even morally safer, but at least peopled by co-religionists which apparently made extortion, temptation, and vice more acceptable! A local university without religious test was sorely needed in Ulster. Primate Robinson (Baron Rokeby) planned one for Armagh and left some handsome buildings and £5,000 in his will in 1796 to endow it. His dead hand held the purse since the offer was to lapse after five years.[9] Government's interest in the scheme, initially aroused, was blown away two years later by the guns of the '98. Presbyterians therefore had to go it alone. They responded by building a non-denominational 'academical institution' in Belfast (incorporated by Act of Parliament in 1810) to be part boys' school ('the primary department'), part a composite further education college and university college ('the College department'); broadly a Scottish university in embryo with an extra-mural department and a school tacked on.[10, 11]The 'College department', through a faculty of arts, awarded a three-year general certificate and also ran classes (for part-time and occasional students) of 'popular lectures upon those subjects which are most conducive to the improvement of the Agriculture, Arts, and Manufactures of this country'.[12] A faculty of medicine was also planned, with the intention that its certificate would be recognised by the main licensing bodies for acceptance to sit their final ('licensing') examinations. The founders, naïvely optimistic, supposed that a university charter would follow and Inst be enabled to award its own degrees. Their hopes were to be dashed; like the similarly rebuffed Newman's College (or 'Catholic University') in Dublin 40 years later, Inst was not in government favour, and it acted out its entire collegiate existence as a mere 'preparatory' (i.e. non-degree-giving) body. It remained staunchly non-denominational: Thomas O'Hagan, first Catholic Lord Chancellor of Ireland, was schooled at Inst; John Gavan Duffy attended lectures in the College department; and Bishop Crolly, Catholic Bishop of Down and Connor, was a proprietor and subscribed over £100 to found it. Many Anglicans also subscribed and enrolled. But most students, proprietors, and Inst's ethos were Presbyterian, *viz.* secular education taken in common; religious instruction taken separately; self-

improvement, diligence, providence and self-control the cardinal virtues; and an evangelical assumption that attaining goods in this world and salvation in the next would be the rewards of virtue! The uncompromising slogan on prize medals was 'work is everything'; the motto was (and is) 'seek the truth'. Dr William Drennan MD, the veteran United Irishman, gave the opening address on 1st February 1814 which encapsulated the educational and vocational intentions of the founders — 'It is intended to diffuse as widely as possible through the province and population of Ulster the benefits of Education both useful and liberal'; and also their pragmatic objective of retaining their sons in Ulster — 'The Academical Institution will prevent the hard and disgraceful necessity . . . of parents sending their children to seek in other countries, with much risk to their health and morals, for that instruction . . . which might be equally well attained at home with evident advantage to the public interest as well as to that of individuals'.[13] Medicine was to start at once by creating two pre-clinical chairs — botany, and anatomy and medical physiology. But at once disaster struck: staff and proprietors were reported drinking seditious toasts at a St Patrick's Day banquet in Gillet's Tavern in 1816 ('to Marshal Ney' and 'to an early reform of the franchise' are fair examples). Government now sought assurances on loyal behaviour and greater proprietorial control to enforce them. It failed to get these and withdrew its grant of £1,500 p.a. Medical school plans were now shelved, but an unsung hero, James Lawson Drummond MD, took the ill-paid (£50 p.a.) chair of anatomy and medical physiology in 1819 and also that of botany in 1822, teaching these subjects to arts and theology students mainly to keep the pre-clinical nucleus of a future medical school alive. He had a long 15 years to wait. (Fig 1).

Fig 1. James Lawson Drummond (1783 – 1853), first dean of the RBAI faculty of medicine board. From an engraved portrait in the Ulster Museum and reproduced by courtesy of the Trustees.

Meanwhile back at the Belfast Fever Hospital things looked brighter. The hospital itself was a legacy to a remarkable group of men — principally James McDonnell MD. McDonnell bestrode contemporary Belfast: patriot and polymath, member of a cadet branch of the McDonnells of the Glens, the hereditary earls of Antrim; the man who revived in Belfast the ideals of the Granard Harp Festivals, who prodded Edward Bunting to compile his musical anthologies, who helped found the Belfast Literary Society and the Belfast Reading Society, who revived the Belfast (now the Ulster) Medical Society; the *confidante* and patron of Thomas Russell, though ultimately one of his self-confessed betrayers; the friend and host of Wolfe Tone, whom Tone linked in his *Diary* with Russell, Whitley Stokes, Simms, Neilson, Napper Tandy and others of his inner circle, giving McDonnell one of his rare and treasured *soubriquets*—'the hypocrite' (not, I should

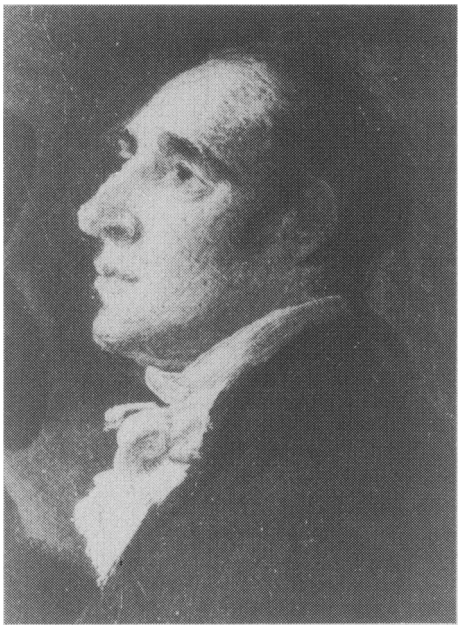

Fig 2. James McDonnell (1763-1845). Detail from *The entry of Lord Hardwick into Belfast as Lord Lieutenant, 27 August 1804,* a composite picture by Thomas Robinson, reproduced by kind permission of the Belfast Harbour Commissioners. (Photo: Norman McMullan).

say, literally, but presumably after Hippocrates); and the driving force behind the foundation of the Belfast Fever Hospital and Dispensary in 1792 which after small beginnings and fluctuating fortunes re-opened in Frederick Street in 1817 with over 100 beds. (Fig 2). 'The Nobility, Ladies and Gentlemen of Belfast and its Vicinity' showed their appreciation in a gift of a magnificent ten-piece silver service in 1828 costing the then great sum of £700.[5, 14, 15]

The hospital staff supported the newly-founded Inst; many were in fact proprietors. Their primary loyalty however was to the hospital and they discussed forming a clinical school on the English hospital pattern,[16] independent of Inst and in which students would 'walk the wards' and receive clinical lectures in return for fees. This would give the hospital status and the staff a supply of clerks and dressers and opportunity for patronage. They could leave it to Inst or some other private enterprise to teach the pre-clinical subjects without any formal link. Their autonomy and independence of action would then be ensured. This was a patently narrower view than that held by Inst *viz.* a formally constituted *joint* pre-clinical and clinical school which would ultimately award degrees. All agreed the nobility of Inst's objective, but the hospital staff and committee doubted that it could be reached since Inst was perennially teetering on the brink of bankruptcy and lacked government support. And more than that: Inst with its idealism and high principles was talking of actually *advertising* posts: this might mean that outsiders would get 'chairs' and come looking for beds in the hospital and — worse — would be competing with the hospital staff in their practices! The hospital staff moreover were not repelled by the prevailing practice of patronage and nepotism and would have none of Inst's ideas: they wanted it the other way around, *viz.* to appoint their *own* staff as professors in any joint school. Furthermore, Inst contracts were for five years, the hospital appointments *de jure* were annual, and anyhow a connection with Inst might jeopardise the Grand Jury grant (for fever patients) — the hospital's main source of income. Inst could join them, they had after all Belfast's interests at heart, but only on terms advantageous to the hospital (and themselves), their objects of primary loyalty! And so it was that on 21 December 1821 they went down their own path and enrolled their first student, Mr Walter Bingham, to 'walk the wards' at a one guinea fee.[17] Others followed and on 3 June 1826 McDonnell gave the first formal hospital clinical lecture in what became an identifiable if somewhat limited and irregular series.[1, 2]

Neither Inst nor the hospital saw this as final: indeed it was partly a diplomatic pressure ploy by the latter. Negotiations continued and the next ten years saw

intricate manoeuvring between them: often hard and skilled it was always honest and often altruistic. I have detailed this elsewhere.[1, 2] In the end the joint school idea survived. Compromises were made all round but the thorny principle of open advertisement to professorships and selection by Inst (who would pay them) was preserved, as was Inst's insistence on control of student enrolments and examinations, while the disruptive question of a right to hospital beds was shelved and was to be a source of controversy into living memory! With harmony restored, the Inst visionaries raised money for buildings, drafted a scheme for the joint school and a four-year syllabus which was positively enlightened, and in 1835 — 20 years after Inst opened and exactly 150 years ago — the Faculty of Medicine was established with five of the planned twelve professors in post, and with J.L. Drummond as dean ('President of the Board of Faculty of the Medical Department'). The Faculty held its first meeting on 8 October 1835, 14 years before the Queen's Colleges in Cork and Galway (and Belfast) opened. Moreover, this was no brainchild of unschooled provincials in some remote hamlet: it was devised by high-minded and liberal men and was by far the most 'modern' of the dozen or so provincial schools in the kingdom, while Belfast itself was now a thriving industrial port of 65,000 with a prosperous hinterland. The joint school was free from hospital staff control — unlike provincial schools in England. It was free from town council control — unlike Edinburgh. It was free from control of professional bodies — unlike Glasgow. It was a true partnership between an incorporated autonomous college and a voluntary hospital — a structural prototype (barring some constitutional niceties) of the modern medical school. (Fig 3).

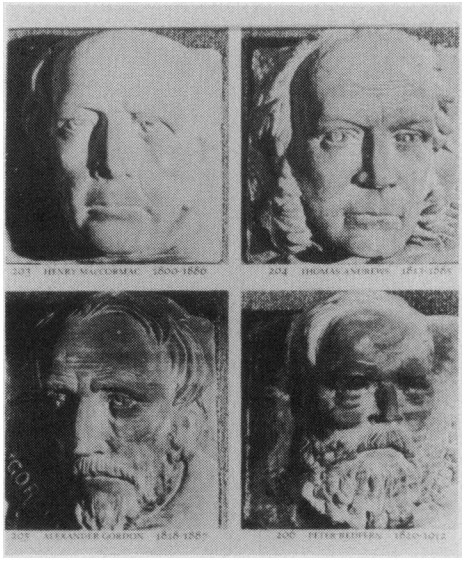

Fig 3. Terracotta heads of Henry MacCormac (1800-1886), Thomas Andrews (1813-1885), Alexander Gordon (1818-1887) and Peter Redfern (1820-1912). These were formerly part of the decoration of the (Whitla) Medical Institute in College Square North and since 1976 have been displayed in the concourse of the Whitla Building, QUB, as part of the UMS memorabilia.

*Progress*

The school was on the whole successful. Most of the major licensing bodies soon approved its course. Enrolments were buoyant — some 400-500 enrolled in its 14 years making it one of the bigger provincial schools. The curriculum was quickly consolidated and only the ambitious but misconceived episode of the purchase of the Old Cavalry Barracks in Barrack Street and its attempted conversion into a 100-bed 'teaching hospital' — the College Hospital — marred progress.[1, 2] The early 1840s were the zenith. Thereafter lack of capital prevented expansion; the government grant (restored in 1829) was miserly and precluded adequate maintenance and creation of further chairs; even cadavers fell into short supply; and, crucially, the Faculty of Arts crumbled in 1841 with the deep schism in the Ulster Presbyterian Church which Inst, as a main source of ordinands and

rather extravagantly suspect as a centre of 'new light' ideas, could not avoid. The death knell sounded in November 1845 when government decided that the 'northern college' of the (three-college) Queen's University in Ireland would be housed in a new building to the south of the town and not at Inst which the commissioners considered to be too small, too unhealthy because of factory pollution and nearby marshland, too cramped to allow expansion (seven acres), and structurally insecure with sinking foundations. Ironically the bell tolled just as events were moving in the school's favour. In 1847-49 the new 600-bed fever hospital was opened at the Union Workhouse, which meant that more general patients — that is, better clinical material — were admitted to the General Hospital. The Dispensary was reconstituted. And above all Andrew Malcolm joined the hospital staff in 1845 and revitalised the curriculum and teaching methods just as Graves had done on his return to the Meath in 1820 — meticulous case-notes, emphasis on clinical signs and clinical diagnosis, the relating of autopsy findings to the clinical disease, emphasis on the physical over the symptomatic, and instruction in surgical techniques.[18] Malcolm was to die in Dublin ten years later of congestive heart failure at the early age of 38 but into those ten short years he crammed several life-times' activities as writer, teacher, clinician, factory health reformer, philanthropic worker, founder of the Belfast Working Classes Association, editor of the Belfast Peoples' Magazine, secretary of the Belfast Amelioration Society, and much more besides.[19] But it was all too late for Inst; it was Queen's College, Belfast (QCB), which reaped the benefit.

The pioneer work of the joint Inst/hospital school was to give QCB a head-start over its sister colleges in Cork (QCC) and Galway (QCG). In 1849 the Inst students transferred to QCB without loss of credit, and three of the medical professors joined them (William Burden — obstetrics; Alexander Gordon — surgery; John Frederick Hodges — professor of chemistry at Inst, but professor of agriculture at QCB). But this was not quite the end of medical Inst. The Queen's Colleges were not designed initially to house a medical school and so medical students at QCB continued to dissect at Inst until 1863 — one reason why Belfast could take as many as 150 medical students by 1859 while only some ten initially enrolled at QCG. Many of the battles which lay ahead for QCC, QCG, and the Cecilia Street school in Dublin, had already been fought and largely won in Belfast by 1849 and the school was well placed to exploit its new opportunities.

*Opinion*

What influence did this early school have on Irish medicine? Structurally and educationally it showed that such a college/hospital partnership was not only possible but desirable and, furthermore, feasible. Medically it had little: in 14 years little could be expected. A medical school may achieve influence through the export of its graduates, the promulgation of its teaching methods, distinction in research, or by its becoming a Mecca for students and graduates from other schools. Belfast at this time was neither a hive of research activity nor an international Mecca but in common with the other Irish schools it *did* export many of its graduates, possibly 50 per cent. Some did well, then and later; the necessary research to quantify the emigration and identify individuals has yet to be done. There is, however, an old lecture room desk stored at Queen's with the names of 32 undergraduates carved on the top. Eight were of medical men who graduated between 1894 and 1913 — a later period. Of these, three went into practice in

England (Samuel Acheson, Edward Samuel Gorman and James Graham). A fourth entered the RAMC, finishing as a major-general (Samuel Wasson Kyle). A fifth became chief medical officer to the Egyptian State Railway (Campbell Galway Robb). A sixth was medical officer in chief to the Atlantic Fleet (Robert Hunter McGiffen). One is untraced (John Johnston). Only one of the eight practised in Ulster and he with distinction — Sir Robert Johnstone, later professor of gynaecology at Queen's. Earlier experience may not have been dissimilar. But Andrews, and to some extent Drummond, MacCormac and Gordon, were also known through their writings. Thomas Andrews (professor of chemistry) was the leading physical chemist of his day: Fellow and gold medallist of the Royal Society he published his first learned article at the age of 15.[20] He had also studied medicine under Robert Graves at the Meath and imported Graves's clinical methods to Belfast. James Lawson Drummond (professor of anatomy and medical physiology, and of botany) wrote well-used texts.[21, 22] Gordon had work on fractures to his credit.[23] Henry MacCormac (professor of medicine) was a prolific writer over a catholic range and a translator of note. His numerous works, unorganised, ill-based, and often erratic, were nevertheless published for the main part by leading London houses and were well-known. A fresh-air fanatic, he broke the windows of his patients with his cane.[24] His eldest son, Sir William, Bart., was the first Irishman to be president of the Royal College of Surgeons of England. Malcolm was a brilliant systematist and teacher and potentially the most acute observer of them all: his article on flax byssinosis is still a classic.[25] John McDonnell (first professor of surgery), James McDonnell's younger son, has a secure place in Irish surgery. Appointed to Inst in 1835 he resigned after three months on appointment to the Richmond in Dublin and is now remembered as the first surgeon in Ireland to operate using ether anaesthesia — he amputated Mary Kane's arm for septic arthritis of the elbow on New Year's Day, 1847.[14] Robert Little (first professor of midwifery) is an enigma: an active if heterodox and completely uninfluential author in the mid-1830s and an aggressively entrepreneurial if seemingly sound clinician, he emigrated to England in 1840 and relative obscurity returning later to Ireland via a remote cattle station in Australia and lived out the rest of his life in Belfast largely neglected by his colleagues.[3, 4] Most of the rest of the Inst staff (Burden, Coffey, Mateer and Marshall) and Drummond's assistant (1835-7) James Saunders MD, were local worthies who wrote little. (Figs 4 and 5).

They were without exception Irishmen, all except Coffey Ulstermen, but in a unified Ireland they naturally looked to Dublin and its brilliant luminaries for medical leadership and as the fountainhead of ideas. They published mainly in the Dublin journals; many studied in Dublin and/or took the Dublin licences; most respected the Royal Irish Academy and coveted its membership. But they were not dead moons reflecting light from a fiery Dublin sun. They were a discrete and coherent group, even sub-culture, building their own school within their own cultural and scientific *milieu* and their own ethic, character, and standards — a school staffed by regional compatriots, mainly Presbyterian and Anglican of an evangelical cast, and endowed with students enrolled almost exclusively from the fields and streets of Ulster. They cohered early: the Belfast (now Ulster) Medical Society dates from 1806 — one of the original provincial medical societies in these islands — and the Belfast Clinical and Pathological Society was nearly as old. These were practical, hardworking, intensely independent yet compassionate men, serious-minded and with high respect for education and knowledge, often of small rural background and many from the manse,

Fig 4. Robert Coffey (1796-1846), professor of surgery at RBAI, 1837-1846, and attending (from 1826) and consulting (from 1836) surgeon to the Belfast General Hospital.

Fig 5. William Burden (1798-1879), professor of midwifery and diseases of women and children, RBAI (1840-1849) and of midwifery, QCB (1849-1867).

having a deep pride — even conceit — in their own and their society's success. The skills they developed and prized were practical, even frontier ones — they were strong in clinical and observational acumen; stronger still in instructional commitment and ability; weaker on experimental, methodological, or theoretical skills. Intellectually they expressed themselves in theology, law, history, science and medicine; seldom in novels, drama or poetry (a noted exception is William Drennan MD); and their leaders were no exception. The London and Oxbridge physicians and many of the Dublin coterie, with their philosophical and discursive approach, literary pretensions and often success, and their metropolitan pursuits, were far from their world. They were no doubt 'provincial', but, unqualified, this would reflect only part of the whole. In all this they set a pattern for Ulster medicine for the rest of the century, arguably to the present day.

## THE SECOND PERIOD: 1849-1908

### *Progress*

The move to QCB in 1849 ensured the future of the medical school. Inst's precarious finances were now replaced by the assured if modest funding of QCB; government's lukewarm and fickle support for independently conceived Inst (despite the 'Royal' accolade given in 1831) gave way to its unambiguous backing for its own creation, QCB. Furthermore, the three Queen's Colleges constituted a university: students could by right sit the degree examinations of

the Queen's University in Ireland (QUI) instead of hawking their Inst certificate around the licensing bodies of Britain and Ireland for approval and then only as a ticket of admission to the licensing exam. This gave a stability and a platform for growth which was timely: Belfast was growing rapidly — the 75,000 of 1841 became 100,000 in 1851 and was to reach over 200,000 in 1881 and no less than 350,000 in 1901, a staggering growth even for a nineteenth century industrial city. The 55 medical students of 1849 became 327 in 1879. Numbers declined somewhat after that, due partly to the unpopularity of the Dublin-based Royal University of Ireland (RUI) — which replaced QUI in 1881 and was merely an examining body — partly to an increasing exodus of students as steam made travel easier and cheaper and as parents' prosperity increased, and partly no doubt for other reasons as yet unresearched.[26]

The student mix of QCB was largely unchanged from that in Inst. Over the century at least 90 per cent were from Ulster, mostly Belfast, Antrim and Down. Some 65 per cent were Presbyterian; 17 per cent Anglican; 6 per cent Catholic; and 13 per cent 'others'.[26] (Religious affiliation was no longer recorded after 1908 when Queen's University replaced QCB, being prohibited by the QUB charter). This probably represented the religious mix of applicants: there are no grounds to suspect denominational discrimination if for no better reason than that fees were needed and the college was never full! Moreover it was against the QCB ethos. The students carried this geographic and cultural homogeneity into their professional lives giving a cohesion and corporate consciousness to the Belfast medical fraternity and Ulster profession which still exists though with subtleties due to the ever-changing emphases as the religious mix has altered over the years.

Three of the seven Inst medical professors were taken onto the QCB staff (Burden, Gordon and Hodges — see above), thus ensuring a smooth transition: moreover Thomas Andrews had been appointed vice-president in 1845 and so the Inst medical influence at QCB was strong. But, importantly, the replacement of moribund 'collegiate' Inst by the exciting QCB with university college status and wide attraction to potential job applicants introduced a degree of cosmopolitanism into what had been a *de facto* parochial system of staff selection; more precisely, introduced this into the pre-clinical subjects (where problems of hospital beds for outside appointees didn't arise) while perpetuating a virtually closed system in the clinical departments — indeed even more 'closed' than liberal Inst had tolerated. Seven men held the chairs of pathology, anatomy, and physiology in the 60 years of QCB's existence. Two of these were English (Peter Redfern and Johnson Symington); three were Scots (T.H. Milroy, James Smith and William Symmers); one (Hugh Carlile) though an Ulsterman was an *emigré*, having graduated at Trinity College and worked all his life in Dublin; while the seventh (William Thompson) was from Longford and QCG and held the Belfast chair for only nine years before becoming professor of medicine at Trinity. He went down with the torpedoed *Leinster* on 10 October 1918. This cosmopolitanism is in contrast to the tight oligarchical hold on the clinical professorships. Between 1849 and 1947 — 98 years — only two appointments to clinical chairs at QCB and QUB (including materia medica) were made from outside the tight circle of the hospital staff, and each was a special case. John Creery Ferguson was the first: he held the foundation chair of medicine though without a hospital appointment for his first four years (1849-1853). (Fig 6). But he was no exotic import but an Ulsterman from Armagh and considered to be a rare catch for the fledgling QCB since he was professor of medicine at Trinity and formerly professor at

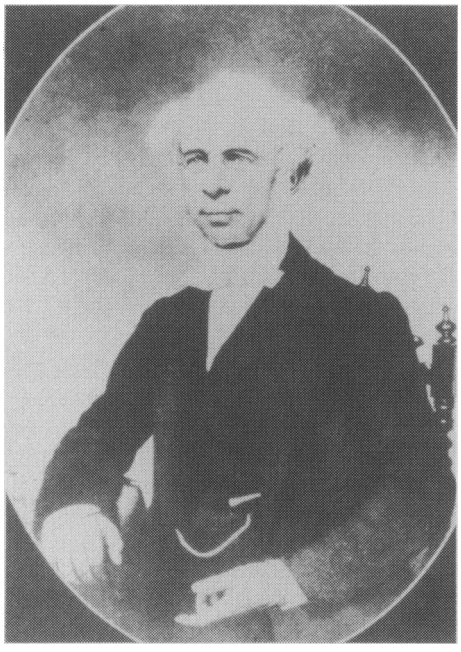

Fig 6. John Creery Ferguson (1802-1865), professor of medicine, QCB (1849-1865) and the only foundation QCB clinical professor not already on the Belfast General Hospital staff when appointed.

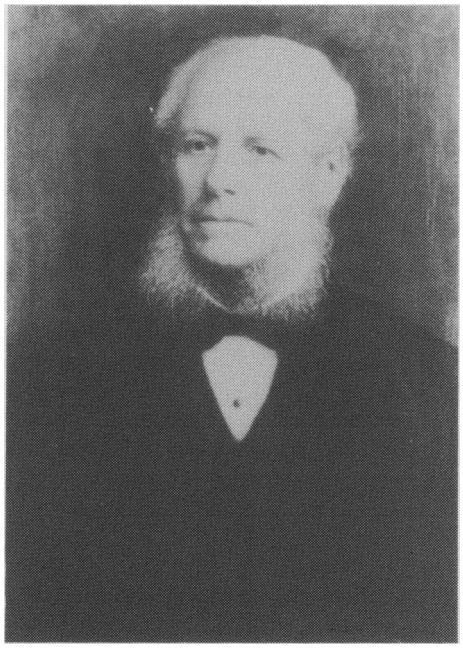

Fig 7. Robert Foster Dill (1811-1893), professor of midwifery, QCB (1868-1893). He had no lying-in hospital post at the time of his appointment. Joined the staff of the Ulster Hospital for Women and Children, 1881. City coroner, 1869-1893.

Apothecaries' Hall.[27] Robert Foster Dill, professor of midwifery 1868-1893, was the other. (Fig 7). Dill belonged to an influential Presbyterian Ulster family of wide and clannish ramifications and used the influence of his cousin, Dr John Dill of Brighton, to press his claim to the chair, successfully, as 'the only conservative candidate' in preference to Dr John M. Pirrie (the QCB president's choice), the then leading Belfast obstetrician and a member of the hospital staff, but a man of well-known liberal associations.[28] Such canvassing was not unusual; indeed it was the custom as the elaborate 'testimonials' for jobs and contemporary reports testify. Professors in the Queen's Colleges were no exception. They were appointed at this time by the Queen (by warrant under the Sign Manual) on the advice of the lord lieutenant — effectively by the chief secretary — on the basis of a priority list prepared by the college president and vice-president who had, however, to justify the ranking. The QCB presidents combined wisdom with pragmatism and *always* recommended a member of the hospital staff, and this reversal of the president's choice was unique in the history of the QCB medical school in Belfast. But Dill had no beds; he had resigned from the Lying-in Hospital some years before. He solved this by taking his students with him on domiciliary confinements and held lectures in his large house in 3 Fisherwick Place.[29] Hospital and college made sure that such mistakes were not repeated!

But though Ferguson and Dill were not, on appointment to chairs, members of the hospital staff, they were still Ulstermen through and through. And Ulsterman meant Ulsterman irrespective of creed. The Catholic Sir Dominic Corrigan found

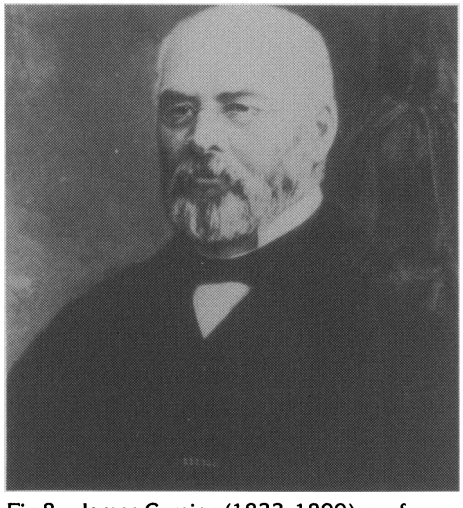

Fig 8. James Cuming (1833-1899), professor of medicine, QCB (1865-1899) and attending physician at the Belfast General Hospital (1865-1899). The only Catholic in the early QCB medical school professoriate.

advancement difficult in a Dublin profession dominated by Protestants.[30] The Catholic James Cuming from Armagh found no such difficulty in a Belfast profession also dominated by Protestants. (Fig 8). He was physician at the hospital for 34 years, professor of medicine at QCB also for 34 years having previously been deputy-professor to Ferguson, not once but twice president of the Ulster Medical Society (1868 and 1881), president of the BMA (1884), and for good measure chairman of the first regular staff committee in the Belfast Royal Hospital.[6] His religion was no bar to his advancement or success: indeed he became the unchallenged doyen of the profession, respected by all; in Andrews's words 'there are few medical men to be found anywhere more highly cultivated or better fitted to fill a chair'.[31]

*Opinion*

This oligarchical control of clinical chairs ensured amicable co-operation between the QCB authorities, the professors, and the hospital staff greatly to the benefit of the school which was cohesive and avoided the disruptive problems of some British schools and the sorry fragmentation of late 19th century Dublin medicine. But there was a price to pay. Generally the professors, though in the main of high clinical skill and probity, were inevitably somewhat provincial in outlook and parochial in experience. Being part-time, they could boast only modest publication lists; their opportunities for foreign study were limited though some made the postgraduate 'grand tour' including Paris, Vienna, Berlin and London. Few undertook lines of systematic research or became ranking authors. There were exceptions, notably Sir William Whitla. Whitla wrote three great books—*Elements of pharmacy, materia medica, and therapeutics* (first published in 1882), *Dictionary of medical treatment* (first published in 1892), and *Manual of practice and theory of medicine* (first published in 1908): the first went through 13 editions up to World War II and the second achieved nine up to 1957 and was translated widely, even into Chinese. These books and successful investments brought him wealth which through his beneficence Queen's enjoys to this day including, I am happy to say, the Vice-Chancellor and his family who live in his substantial house! This parochialism weakened later in the century as circulation of journals, ease of travel, and inclination and the means for foreign study and visits increased: Whitla for one was an inveterate traveller; Lindsay and W.W.D. Thomson were not alone in studying on the continent; and Thomas Sinclair (professor of surgery from 1886 to 1923) was appointed professor at the early age of 28 in preference to the redoubtable Sir John Walton Browne largely because of his several years of study in London, Vienna and Berlin and his holding of what was then unusual in Ulster, the English Fellowship.[6]

Intellectual hybrid vigour also came from another source — expatriates returning from often unusual experiences abroad. Joseph Nelson MD, who became

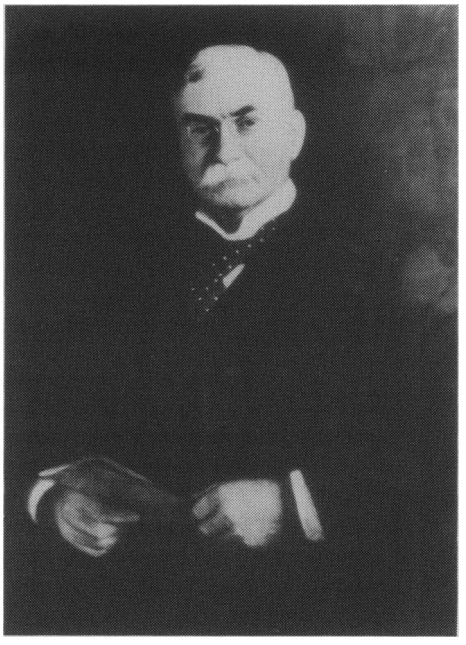

Fig 9. Joseph 'Garibaldi' Nelson (1840-1910). Member of the *Regimento Inglese* and decorated by Garibaldi and Victor Emmanuel. Attending surgeon at the Royal (1882-1906) and founder of the Eye, Ear and Throat Department of RBHSC.

Belfast's leading ophthalmic surgeon in the 1880s and 1890s, left Queen's in 1860 to join Garibaldi's 'Thousand' at Genoa. Commissioned lieutenant in the *Regimento Inglese* he received a rare Sword of Honour from the great man and two medals from King Victor Emmanuel. (Fig 9). He graduated in 1863 (QUI), became for 14 years a tea-planter in India (where he picked up another campaign medal in a punitive expedition against the Muniparis), re-adopted his profession in 1877 by studying ophthalmology in Dublin and Vienna, and returned to Belfast in 1880, joining the hospital staff in 1882 and founding the eye, ear and throat department at the Royal Belfast Hospital for Sick Children. He was inevitably known as 'Garibaldi' Nelson.[6] He was not alone: other *emigrés* returned, or newcomers immigrated, to Belfast lured by its rapidly growing prosperity and the growing status of QCB, and brought welcome cosmopolitan views with them to balance the heavy graduate emigration often of established staff — such as William (later Sir William) MacCormac, Henry's son, who was appointed attending surgeon to the General Hospital in 1865 but made his career in London after serving in the Franco-Prussian War.

But, as the gaze of the profession looked increasingly to London and abroad, just as the gaze of Belfast citizens looked increasingly to Britain and the world, it inevitably swung away from Dublin; indeed it was probably only held there at all by the Dublin-sited RUI which examined Queen's College students for RUI degrees. Socio-economic and political changes were in any event now distancing Belfast from the rest of Ireland and the decline of medical Dublin only hastened an inevitable estrangement. The English licences became more in evidence; publications once mainly in Irish journals now dotted the pages of English ones. (Of the 65 publications listed to Professor Andrew Fullerton between 1891 and 1933, four appeared in *Irish Journal of Medical Science,* five in Ulster journals or through Ulster publishers, one in a Canadian journal and the rest in British ones. Several were in *Medical Press and Circular,* originally published in Dublin but from 1869 in London. Some of the 'shift' is no doubt due to the decline of Dublin as a medical publishing centre). And with all this was a growing self-confidence as the school became a leading one in the British Isles, the equal — even (they would have argued) the superior — of sadly fragmented and politically embroiled Dublin and far ahead of QCC and QCG which lacked what QCB so spectacularly did not, local support and confidence. In 1850 only the 100 beds in the General Hospital were available to Queen's, but in the next 50 years the Union Hospital, the Mater Infirmorum, and the growing number of specialist hospitals for diseases of the

eye, ear, skin, for children, midwifery, and mental diseases, gave to QCB a supply of clinical beds hardly equalled elsewhere. Whitla in his presidential address to the BMA in 1909 could list some 1800 beds in general hospitals and nearly 200 in specialist non-mental hospitals in Belfast alone 'which were', in his words, 'from time to time in late years utilised by the students attending our Medical School'.[32]

Belfast in fact was booming and was becoming locked into the Union, and Ulster was growing increasingly remote from the rest of Ireland. Few Belfastmen now went south to practise, if they ever did, though some joined Irish government service centred in Dublin — like the surgeon John (later Sir John) Fagan, chief surgeon at the hospital who left in 1897 to become Inspector of Reformatory and Industrial Schools in Ireland but only under the stimulus of what R.S. Allison calls 'an unfortunate and sad mistake in operating'[33] and which the late Charles Dickson always told me was an amputation of a wrong (and healthy) leg. The first practising Ulster surgeon to be president of RCSI was Andrew Fullerton in 1926-28 and 1929-30; and the first practising Ulster physician to be president of RCPI was Dr Alan Grant in 1979. The entire nineteenth century saw no Belfast-based Irish College presidents, but I doubt whether the fraternity in Belfast after about 1860 cared much about that. They were by now very much their own men and Dublin no longer their unarguable Mecca or metropolis.

## THE THIRD AND FOURTH PERIODS: 1908-1948, AND 1948 TO THE PRESENT

### *Progress*

In 1908 the Irish universities were again reorganised into a form which has lasted to the present day. QCB now became a university, the unchallenged intellectual centre of Ulster with status appropriate to Edwardian Belfast, the Kingdom's eighth city now of equal size and wealth to Dublin. From hardly more than a fortified fishing port to over 400,000 souls in a century and a half with the largest weaving and tobacco factories, ropeworks, and output of shipping in the world, was a near miracle by the 'self-made men in the self-made city'.[34] This success showed, rather too obviously at times, in the supreme confidence of its citizens in the future of the city and of self, verging all too often on arrogance and complacency. But the most obvious change in QUB during the present century is in size. The modest 620 students in 1909 doubled in a decade and reached nearly 3,000 in 1950. They are now 7,500. The medical school had 282 pupils in 1909 but nearly 800 in 1950 and only government restriction and lack of resources has prevented growth to 1,000 or more. The medical school was strengthened through increase in the number of chairs, and made even more cohesive by the appointment of full-time university lecturers and part-time clinical lecturers and examiners drawn from the staff of the teaching hospitals and backed by extension of the clinical teacher system whereby consultants taught students in ward and out-patients as they had always done, reimbursed (increasingly nominally!) from student fees which from 1957 were channelled through QUB. The partition of Ireland widened the pre-existing gap between Belfast and the other Irish medical centres and this became a yawning chasm after the introduction of the National Health Service (NHS) in 1948 (which at first the Mater Infirmorum Hospital 'disclaimed' though it remained a teaching hospital and an integral and important cog in the comprehensive health care wheel) when full-time professorial clinical units were established, medical and paramedical infra-structures were

expanded, and the Province's hospitals were improved and updated and new ones built. In hospital standards, in level of staffing, in quality of professoriate, in research now burgeoning with the appointment of full-time academic staff, and in international standing, the Belfast school was in the 1950s at its zenith, a zenith thrown into more vivid relief as the doldrums into which the southern Irish schools of the pre-World War I period had drifted positively becalmed them under the social and political circumstances of the 1920s, '30s and '40s.

Up to 1948, QUB and its teaching hospitals have continued to practise that enlightened pragmatism in clinical professorial appointments which had ensured mutual institutional peace, the profession's cohesion, and perhaps even the school's survival over the previous century, but the advent of the new NHS now gave responsibility for hospital management (and bed allocation) and staff appointments to government agencies, and it was possible for QUB to contemplate appointing non-Belfast clinical professors for the first time in the school's existence. Most of the chairs in pre- and para-clinical subjects continued to be filled by non-Irishmen: 12 of the 14 professors appointed in these subjects between 1920 and 1950 were from outside Ulster, evidence of a growing internationalism and an intensification of previous practice where hospital facilities were not an issue. In 1947 this openness was extended to clinical chairs with the appointment of the Englishman Harold Rodgers to the chair of surgery. This underscored the British orientation of the school which had been growing since the mid-19th century. The diplomas of the Irish Royal Colleges yielded almost completely to those of London and Edinburgh as primary postgraduate objectives; indeed frequently they were never even sought and their possession often bestowed no career advantage. Few senior staff supported the Royal Academy of Medicine, appeared on Dublin platforms, sought advancement in the Irish Royal Colleges or published in Dublin journals — though there were notable exceptions like QUB pre-clinical scientists publishing extensively in the *Irish Journal of Medical Science,* and Sir Ian Fraser who was president of the RCSI in 1954-56 and a lifelong advocate of involvement by Ulster doctors in Irish professional affairs. When I joined QUB some 30 years ago the gulf between the Belfast and Dublin professions was nearly unbridged except through the activities of some individuals and perhaps through examining in the medical schools and the Royal Colleges. Indeed this mutual disinterest did little credit to either fraternity and those who tried to build bridges often got scant encouragement from their colleagues.

Since the 1950s, however, there has been a radical and welcome change. The appointment to clinical chairs from outside the Province has continued, even quickened: of the 29 clinical and laboratory professorial department heads appointed 1948-82, 11 have been non-Ulstermen and women and most of the remaining 18 received much of their postgraduate experience outside Ireland in stark contrast to the period 1835-1947.[6] Harold Rodgers's (1947) and (Sir) Graham Bull's (1951) appointments had been the start of a trend, not isolated phenomena. And concomitant with this has been a growing *détente* between the Belfast and Dublin professions. The great advance in hospital provision and the creation of full-time clinical professorial units in the Republic (though these are not exactly equivalent to the 'full-time' units in the UK model) have narrowed the gap in academic standards which was previously all too wide: indeed in some subjects the gap may no longer exist. Social and economic disparities are disappearing, at least so far as the eastern regions of the two parts of Ireland are concerned and recent hospital building plans and amalgamations will further

enhance clinical standards. In 1972 the Mater Infirmorum accepted terms which allowed it to join the NHS thereby ensuring cohesiveness and removing an ongoing unsatisfactory situation which the good sense and professional probity of its staff had kept from becoming other than an exaggerated issue. In the political context of the time it was widely seen as a conciliatory gesture all round. The work of pioneers to bring the northern and southern fraternities into closer association has started to bear fruit: the Corrigan Club, now over 20 years old, is only one of many such initiatives. European politics has helped: the rejuvenation of the Irish Royal Colleges, due in part to opportunities afforded by the European Community, has reawoken the interest of Belfast doctors in the Colleges' position and affairs and we have recently seen an Ulster president in Kildare Street (Dr Alan Grant), one to succeed Mr Victor Lane in St Stephen's Green (Mr Reggie Magee), and for good measure another to preside over the Royal Academy of Medicine in Ireland (Professor Ian Roddie). Medical education has helped also: the formation of national faculties and 'new' professional colleges has widened the scope for national involvement and the Ulster doctors have responded wholeheartedly and in the main with success and unfailing encouragement. Furthermore, for the last decade the *ad eundem* fellowships of the Irish Royal Colleges have been sought and respected by Ulstermen, as have the periodic visits to Belfast of RCSI — its first, incidentally, was in 1977, 193 years after its foundation, so perhaps growing estrangement up to 1950 was not all our fault! I believe southern doctors, certainly from the medical schools and teaching hospitals, have reciprocated wholeheartedly to reawakened Ulster interest and are as keen as any to cultivate these relationships. Communications have played a part: the motor car has reduced the 100 miles from Belfast to Dublin to two hours of convenience from the nearly two days of discomfort of 150 years ago. Politics however have not helped. Inevitably the tensions of the past 15 years have taken their toll among some of the rank and file and even a leader or two, but in the main the northern and southern professions have a greater sense of common purpose and objective and are on better mutual terms than at any time since the rise of Ulster unionism and of the southern 'Repeal' and Home Rule movements over a century ago. No longer would a knighthood be denied to any Ulster president of the Royal College of Surgeons in Ireland for seeming to question the wisdom of 'the border', as allegedly it was denied to Andy Fullerton for having his presidential words 'in the field of surgery there should be no border' misreported in the Belfast newspapers as 'Famous Belfast surgeon says there should be no border'![35] I like to think that both in the scientific and professional fields the successive Belfast schools of medicine have played a role in Irish and world medicine disproportionate to their size and that of the Province, and that their structure, standards and regulation have set a high example for any school in these islands and beyond.

*Opinion*

Drawing on this scenario, how can we describe the distinctive features of Ulster medicine?

*Firstly,* in its practice. Ulster medicine is the heir to a pragmatic and clinically orientated tradition, an inevitable and wholly laudable ethos whose genesis lies in the sense of values of the Ulster society which spawned it. (This society, though unquestionably Irish, is in Estyn Evans's words a 'strong regional variant in habitat, heritage and history'[36] — a description which F.S.L. Lyons considered 'the most balanced view available to us'.[37]). Such a society required and applauded practical, even artisan, abilities, and provided the robust, puritan, and

unsophisticated *milieu* of a rural, even frontier, composition with its accompanying social structure, demands on character, and political perceptions. Certainly at its grassroots and even in its educated classes, such a society had also little time for philosophising or for effecting the metropolitan graces and *mores* of territorial grandees, establishment placemen, or a sophisticated urban bourgeoisie, and its medical sons mostly reacted likewise. Clinical and ethical standards have always been high as has educative commitment; investigative enthusiasm (and accompanying research success) less so. There have of course been exceptions — Andrews, Redfern, MacCormac, Whitla, Fullerton, Walmsley, and others enjoyed wide and deserved reputations through their writings, and some contemporaries are particularly successful and prolific though this article is not their story — but clinical skills remained the centre piece certainly up to 1948 and arguably still to-day as judged by the local fraternity's ranking of professional values and its continuing heavy emphasis on clinical instruction. Few external examiners leave without commenting on the clinical abilities and awareness of the students, and until the syllabus was shortened our four undergraduate clinical years were, almost alone in the UK, considered essential. The remarkable achievements of the Belfast hospitals and practitioners in the recent civil emergencies, widely regarded and rightly so to evidence their depth of clinical skill and commitment, in turn have enabled them to withstand unusual pressures in a way which is the envy of colleagues elsewhere.

Research, while perhaps not the brightest jewel in our diadem, is certainly not wanting, at least not since the creation of the full-time clinical academic units. We have many distinguished primary researchers and university centres of excellence, but existing evidence, such as it is, indicates a lower general reputation in published research than in other facets of the art.[38] I can hear the pack of lecturers and professors, myself included, baying at my heels, but evidence is accumulating that this statement is correct, or perhaps perceived to be correct, which is equally damaging! One aspect of our research activity, however, is significant if not unique: our full-time clinical colleagues have contributed to the total research effort of the school to a degree I think unequalled in these islands. It is in fact one of the more remarkable aspects of contemporary Ulster medicine. It would be invidious though tempting to single out stars from what is a galaxy but the fact that Belfast's distinguished acute coronary care, renal transplant, endocrine, surgical gastro-enterological, dermatological, neonatal pathological, and neurological and neuro-surgical units have reached pre-eminence mainly (though certainly not exclusively) without *formal* university connection — and if these are the best units they are not the only ones — emphasises both the remarkable skills the Ulster profession deploys and our historic emphasis on clinical-led research which has enabled these and other specialties to develop from observations in the clinical situation and at the bedside. In baldly saying this I am not setting up an adversarial university versus NHS comparison: much of the research appetite and skills among NHS staff were developed by precept and example from their (usually QUB) teachers, and many were and are stimulated and assisted by university staff.

*Second,* in its high-minded adherence to the tradition of our profession as teachers. Imparting and seeking knowledge were characteristics of particularly Presbyterianism in the earlier days of the school and were powerful facets of the new awakening in the early 19th century which was perhaps one of the most exciting periods in Belfast's history. Inst and the hospital were founded at the very

height of this great burst of enthusiasm for enquiry, enquiry into anything and everything from national culture and heritage, through indigenous fauna and flora, to the wonders of the new factory machines, and all blended with a puritan austerity to produce a disciplined intellectual vigour which ensured that many leading medical men were also prominent in the general scientific and cultural life of Belfast — of the pioneers, McDonnell, Drummond, Marshall, MacCormac, Andrews, Drennan, spring at once to mind. Most of our learned and cultural societies date from this period including the Ulster (then Belfast) Medical Society in 1806. Indeed Belfast came close to generating a modest *cadre* of Renaissance men: close to it but not quite there; social structures, priorities, and geography got in the way and our medical school became filled with the sons of Ulster's small farmers and tradesmen to whom the practicalities not the abstractions of life were all-important and whose Victorian evangelicalism inspired in them a belief in the virtues of application in this world to obtain salvation in the next! Some were innovative researchers and creative thinkers, but they were few; and early Belfast medicine had in retrospect probably only Andrews (and largely for chemistry), McDonnell, and Malcolm of undoubted questioning genius to rival Stokes, Graves, Corrigan and the other major luminaries of the contemporary Dublin school. This emphasis on instruction as a professional duty and vocational ethic is still strong in Belfast — Biggart, Thomson, Rodgers, Walmsley, Pritchard, Macafee, Graham Bull, and many others, will be remembered as teachers after their contributions to the literature, however worthy, have faded. And in none is this vocational ethic more strongly developed than in the *corps* of clinical teachers and the activities of the postgraduate medical education council.

*Third,* in the compassion and commitment of its practitioners. Good and bad doctors abound in all societies and we have our share of both, but in Ulster there is an added dimension of a common cultural and historical identity between doctors and those among whom they practise. Ulster's doctors were never Oxbridge or Pall Mall gentlemen, younger sons of noble or patrician families who owed their physician's rank to high birth or their surgical advancement to the cruder excesses of patronage and nepotism, and there was no great social or cultural gulf between themselves and those they tended. Nor were they the exclusive oligarchy of the Dublin Anglo-Irish minority, albeit a brilliant one. No; they and their patients were of the fields and streets of Ulster, of common culture and heritage, and they saw themselves as equals divided only by the skills they possessed. If such cultural identity has led to patients seeking as their practitioners co-religionists it has merely fortified the historic cohesion but this is no place to develop wider aspects of this debate.

*Fourth,* in the coherence and cohesion of the profession. In our whole history the great majority of students have been from Ulster and until the last 40 years nearly all our clinical staff in university and hospitals have been from Ulster also and moreover have been our own graduates, and this persists noticeably in general practice up to to-day. In-breeding can be vitiating and harmful, but I believe that up to at least 15 years ago the amount of hybrid vigour from imports was adequate compensation. Imports have declined recently for obvious reasons and if I detect a potential source of weakness for the future it is in this very factor of excessive self-perpetuation especially in our university research activities where, I have already noted, effects are even now being felt.[38]

Yet the in-breeding and self-fertilisation, while not necessarily of themselves desirable, testify to a remarkable basic strength. For 150 years the profession in

Ulster has been largely replenished from its own stock and outside non-clinical *academe* from its own medical school and I would question whether many regions or provinces could do so over so long a period without serious detriment to standards. By any criteria of assessment the school and the Ulster profession thrive, a great credit to all since they are largely taught by and base themselves on compatriots and graduates. The local profession has in fact generation after generation thrown up those capable of high professional and academic office both at home and abroad. This must be the litmus test of the secure basis on which the Ulster profession is founded.

In fact it is this very cohesion that made for the success of our medical school and, as a by-product, made the joint appointment system possible. In Britain, academic clinical staff would often be considered outsiders by the hospital patients — and even staff! They tend the sick as honorary consultants and inevitably friction can result between them and the NHS consultant staff who are employees of the Health Board. Not so likely in Northern Ireland, where academic staff are jointly employed by university and Health Board, and in 1948 it seemed the most natural thing in the world to cement school and hospital relations further through this joint appointment system. Though national developments are placing it under some strain, the system should survive if for no other reason than that here in Belfast it merely formalises a relationship which has existed for 150 years. John Henry Biggart in his wisdom, to which the president referred in his address which opened the session,[39] saw this as an axiom, and I feel sure that most agree with this judgement, and that most Ulster doctors conscious of their heritage would have agreed with Sir John's decision to develop a system in keeping with our history and tradition in preference to one devised for the culturally, historically, and structurally very different jurisdictions across the Irish Sea. The system has withstood special studies chaired by distinguished outsiders including the late Lord Cohen of Birkenhead and, if it should pass, something of our traditional cohesion will be lost, and whatever replaces it will have to be very good indeed.

My thanks go to Dr John Weaver who invited me to contribute to the 1984-85 programme. My clerical and secretarial staff again tolerated my eccentricities and unreasonable demands. Mr Watson maintained his customary standard in preparing the illustrations. But my greatest debt is to those whose writings have provided me with both invaluable information and stimulating example. Regrettably, only a few appear in the limited list of references accompanying this paper.

## ILLUSTRATIONS

Faced with an *embarras de choix* I have selected likenesses, which are rarely published, of some of those doctors who played an important part in the development of the early school. A comprehensive catalogue of known portraits of late Ulster doctors of standing is given in reference no. 6, pp. 287-8, and many are reproduced in my chapter in that book (pp. 183-213). Material concerning the early Faculty, curriculum, buildings, Old Barrack Hospital, and cognate matters relating to the early school are in my articles referenced opposite (nos. 1-5, 7, 14, 15).

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 109 – 121, October 1985.*

# Ageing in the 80s

The Robert Campbell Oration
delivered to the Ulster Medical Society, 10 January 1985.

Robert W Stout

It is a great honour to be invited to deliver the Robert Campbell Oration and a humbling experience to inspect the list of previous Campbell orators. Robert Campbell was one of the major figures of Belfast medicine in the early years of this century.[1] He was surgeon to both the Children's Hospital and the Royal Victoria Hospital and pioneered many surgical measures which we now take for granted. He was the first in Ulster to adopt in its entirety the system of aseptic surgery, was an early user of rubber gloves, and the first in Ulster to advocate the use of face masks covering the mouth and nose during operations. His most important contributions were in the operative treatment of hernias in infants and children, and in diagnosing different types of acute appendicitis.

He was also a notable teacher. At an early stage of the preparation of this address I came across some remarks he made on lectures. 'Courses of lectures are relics of the days when printing was in its infancy and treatises of medical subjects were few and far between. Nowadays books are published yearly on every subject in the medical curriculum, most of which contain in readable form the greater part of the material professors and lecturers grind out in mechanical fashion in session after session'. I have to say that at that stage in the preparation of this lecture I found myself in sympathy with his sentiments. He goes on to say that 'lectures . . . . should be confined to the discussion of subjects about which some recent information, not yet embodied in the handbooks, could be given and to the elucidation of difficult points which could be more clearly expressed by oral teaching'. He believed that this plan would reduce the number of lectures by four fifths and that the time saved could be spent on clinical instruction in hospital. There is a very modern ring to these sentiments and curriculum planners are still trying to find the correct balance between didactic teaching and clinical instruction.

In the spirit of Robert Campbell's strictures on lectures I shall try to relate some more recent information on the subject of ageing. I plan to discuss some developing knowledge in the field of ageing, to identify some questions which need to be answered and to mention some of the research which has been carried out in the Queen's University Department of Geriatric Medicine.

## THE AGEING POPULATION

It is customary to start a discussion on ageing and the elderly by noting the increasing number of old people in our society. The important points are the number of old people in the community at present, the proportion of the population which is occupied by old people, the fact that the very old are

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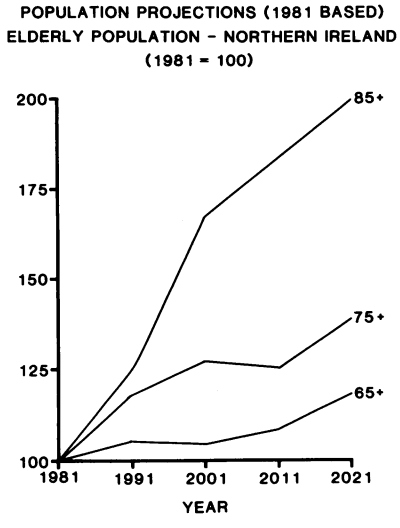


Fig 1. Population projections for the elderly population in Northern Ireland (Based on 1981 population which is taken as 100).

increasing in number even more rapidly than those in the early years after retirement and that this trend is going to continue for at least the next four decades (Fig 1). Why is there so much interest in this information? It is its implications which are of particular concern. It is sometimes suggested that our society is about to be overwhelmed by a tidal wave of frail elderly people who will ruin our economy by their need for pensions and other financial support and who will virtually take over all our health and social services resources. Phrases like 'the rising tide',[2] 'the quiet epidemic'[3] and 'the impending crisis'[4] are common in the geriatric literature. Should we be worried about the ageing population? Or will other developments occur to change the picture?

Patterns of human survival have changed greatly over the centuries. There has been a very marked fall in mortality in infancy and childhood with a much greater survival into old age (Fig 2). However, the maximum length of time for which a human can survive has not altered appreciably, and hence the survival curve is tending towards a rectangular shape. An implication of the 'rectangularisation' of the survival curve is that there is a ceiling to life expectancy and that biological constraints on the human lifespan will limit further increases in life expectancy.[5, 6, 7]

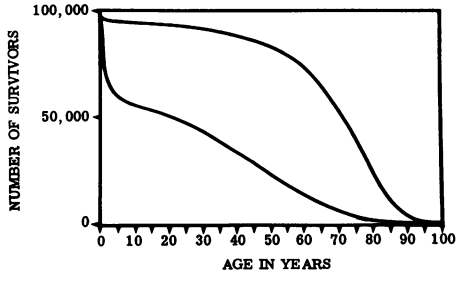


Fig 2. Survival curves. The lower curve represents the pattern of survival in developed countries in previous centuries. There is a high mortality in early life with very few surviving into old age. The upper curve represents survival in developed countries today. There is now a much lower mortality in early life with the majority of people surviving into old age. Nevertheless the age of maximum survival has not changed.

It is often suggested that medical discoveries and social advances have increased the survival into old age of younger people but have had virtually no impact on health or survival in old age. Close inspection of recent population statistics shows that this is not so. In recent years the survival of the very old has increased and mortality rates even in centenarians have decreased.[8, 9] As a result the number of old people aged 100 and over has steadily increased in the last 30 years both in Great Britain and in Northern Ireland (Fig 3).

These changes could be interpreted in two ways. One is that more people are surviving to the end of the human lifespan which is somewhere around 110. The other is that life expectancy is continuing to be pushed outwards, albeit more slowly in the older age groups than in younger people. It seems that the previous idea of a human lifespan fixed at 110 years may have to be modified. Whichever

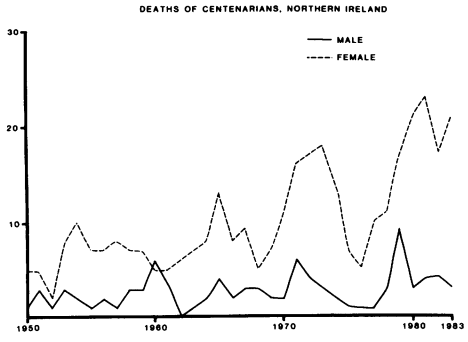


Fig 3. Deaths of centenarians in Northern Ireland 1950 – 1983 (Drawn from data kindly supplied by the Registrar General, Northern Ireland).

interpretation is correct, a reduction in mortality of very old people will have a major impact on the age structure of the country and on the demand for services for the elderly.

## AGEING MEN AND WOMEN

One of the striking features of the older population is the progressively increasing proportion of women. This is present in all developed countries, but has only been evident this century. Life expectancy in women is about six years longer than that in men. There are two possible explanations for the greater survival in women: women may be biologically fitter than men, or men may behave in ways which are more damaging to their health. If the latter is true, then it may be possible to decrease the difference in life expectancy.

What evidence is there for these explanations? Until recently one of the most striking differences in behaviour between men and women was in smoking habits. Evidence that smoking may shorten life expectancy in men has come from studies of groups of people who for cultural or religious reasons do not smoke. In these communities the difference in life expectancy between men and women is very much less than in the population as a whole, although the difference is not totally eliminated [10, 11, 12] (Table I). It is estimated that about half the difference in life expectancy between men and women can be accounted for by differences in smoking habits.

TABLE I

*Life expectancy in the general population of the USA and in three groups of non-smokers* [10]

| | *Life expectancy* | | |
|---|---|---|---|
| | *Males* | *Females* | *Difference* |
| USA — 1970 | 71.5 | 78.0 | 6.5 |
| California Adventists | 78.0 | 81.2 | 3.2 |
| California Mormons 1968-75 | 76.5 | 79.9 | 3.4 |
| USA — Non-smokers 1966-68 | 74.6 | 78.8 | 4.2 |

Surprisingly there have been very few studies directed to biological differences between men and women in old age. In most studies of ageing, men and women have been grouped together for analysis. However, studies carried out in Belfast have identified some differences in elderly men and women. Dr Girvan McConnell, when investigating the mechanism of glucose intolerance in the elderly, studied groups of elderly men and elderly women as well as young men and young women and measured the blood levels of a number of different hormones related to carbohydrate metabolism.[13] He found significant differences between men and women in some of these hormones, for example, gastric inhibitory polypeptide (GIP) (Fig 4), a hormone related to insulin secretion.

Dr Maeve Rea has been studying neutrophil function which may be related to the resistance of the individual to disease[14] and has identified differences between older males and females in phagocytosis, differences which might be advantageous to females (Fig 5). The biological significance of these findings is not clear at present but they indicate a need for further research into physiological and pathological differences in older men and women. The difference in survival between men and women is probably due to a combination of behavioural and biological differences. Thus the male may be biologically predisposed to more serious effects from behavioural changes than the female.

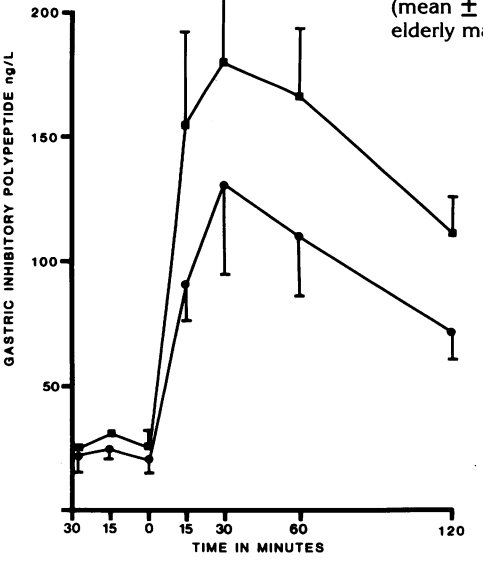


Fig 4 (left). Gastric inhibitory polypeptide (GIP) responses (mean ± SEM) during 50 g oral glucose tolerance tests in elderly males (circles) and females (squares).[13]

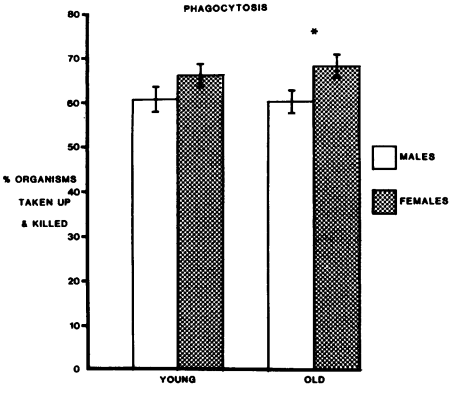


Fig 5 (above). Phagocytosis by neutrophils from healthy young males and females and elderly males and females (mean ± SEM *indicates statistically significant difference).[14]

In this respect it is interesting to look again at the mortality of centenarians. If mortality is recalculated in relation to the number of people alive at age 100, mortality rates are the same in men and women (Fig 6). Thus, it appears that men have a dangerous period of life in their 70s and 80s but, if they survive this, their mortality rates are the same as those of women.

The difference in life expectancy in men and women is not merely a theoretical consideration but is of considerable practical importance. One result of the differential mortality is an imbalance in the numbers of widows and widowers. Apart from the personal problems this causes it has an impact on hospital stay as not only are more unmarried people admitted to hospital, their length of stay is about twice that of married people of the same age.[15] Thus, in an effort to tackle ageing in relation to survival, ageing men appear to be a prime target.

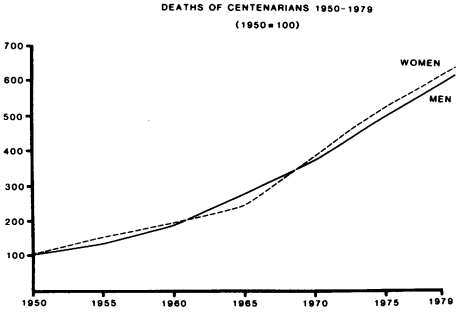


Fig 6. Relative mortality of centenarians 1950-1979. Mortality in males and females in 1950 is taken as 100. (Calculated from data in reference 8).

## PHYSICAL AGEING

The obvious physical changes of ageing are well known. Less obvious is the decline in function of multiple organs which may be considered in the context of preservation of the response to stress and the maintenance of homoeostasis. Performance is optimal in the twenties and early thirties and then shows a linear decline with much individual variation. The individual not performing at a personal maximum level may improve performance by training, while performance will be decreased temporarily by acute illness or permanently by chronic disease. Reserve function is required when the organism is stressed in order to restore the normal homoeostatic equilibrium. As the reserve of individual organs declines, the ability to maintain homoeostasis in the face of a threat is reduced.

Acute illnesses occur in the elderly but they are not difficult to manage. However, if they occur in an individual with seriously impaired reserves the outcome may be fatal, or if survival occurs it may be at a higher level of dependency. Death results from an imbalance between the host's resistance and the insult to the equilibrium. The lower the reserve capacity, the less the stress required to cause death, and the lower the resistance, the less the importance of the specific nature of the insult. Clinical and pathological observations suggest that a significant number of deaths, perhaps one in four, occur in individuals with minimal organ reserve[16] and hence are essentially natural deaths occurring within a short time of ultimate physiological limits.

## AGE AND CHRONIC DISEASE

The special feature of medicine in older people is the preponderance of chronic disabilities. Chronic disease has different features from acute disease and the approach to it and its management must vary accordingly. The challenge is to deal with disease that cannot be cured, the natural course of which is gradual worsening. The medical aim has to be to slow the rate of progression and to provide forms of assistance to retain a reasonably good quality of life for as long as possible.[17]

At the beginning of this century the major medical problem was infectious disease, with tuberculosis the number one killer. It is the reduction in mortality from infectious and other acute diseases which has led to the present era where the major burdens of illness are chronic diseases. Thus, our successes in combating acute disease have resulted in an increased amount of chronic disease. Because the prevalence of chronic diseases and disabilities depends on both the frequency with which they occur and their average duration, the net effects of successful technical innovation used in disease control has been to raise the prevalence of certain diseases and disabilities.

It is not yet clear whether this era of chronic disease will in its turn slowly decline in significance leaving a third era in which the major health problems will be directly related to the process of ageing. Or whether the survival of many more people into old age will increase the prevalence of chronic disease and the burdens that this will have on people, on society, and on the health and social services.

The chronic diseases do not easily fit into the medical model of diseases with single causes and specific cures. The most common and most serious chronic disease is atherosclerosis which is universal and almost life-long in its course.[18] Atherosclerosis probably develops in the later teens and early twenties and

gradually increases in severity throughout the early and middle adult years although remaining asymptomatic in most people. At some stage the affected artery becomes narrowed sufficiently for symptoms to occur, and the patient goes through what may be described as the clinical horizon, with effects on the heart, brain or lower limbs depending on the artery most affected. It seems unlikely that it will be possible to eliminate the atherosclerotic process itself. The aim must be to delay its progression with postponement of the clinical horizon and its disabling complications. Thus differences between individuals are manifested not by the presence or absence of atherosclerosis but by the rate at which it progresses.

Because atherosclerosis is universal and virtually life-long, life cannot be divided into a pre-atherosclerotic and a post-atherosclerotic phase. However, because there is a symptom threshold, life can be divided into a portion before the threshold is passed and a portion following that threshold. Thus it is reasonable to consider a pre-myocardial infarction or post-infarct phase, or a pre-stroke and a post-stroke phase. The determining factor is the extent and speed of progression of the disease. The question is whether an increase in life expectancy will result in a longer post-stroke or post-infarct phase with its corresponding disability or whether it will be possible to postpone the onset of the clinical horizon. If the clinical horizon can be postponed more rapidly than the increase in life expectancy then the period of terminal infirmity will be shortened.

The goal of medical research is to diminish disease and to enrich life, but in fact we have produced tools which prolong disease and diminish lives and so increase the proportion of people who have disabling or chronic disease. That is a major but unintended effect of many technical improvements stemming from health research.

## PRESENTING FEATURES OF CHRONIC DISEASE IN OLD AGE

The impact of age on the need for services for the elderly is clearly shown in Dr Pamela Gawley's study of geriatric day hospitals in Northern Ireland.[19] The age of the patients attending reaches a peak in the 80s and nearly half the patients are aged 80 and over, a very small proportion of the total elderly population being in this age group (Fig 7). How may chronic disease in old age be approached? First, those conditions which cause most problems must be identified. One problem is delay in discharge from hospital. Dr Pamela Maguire has carried out a survey of nearly 400 patients over 70 years of age admitted

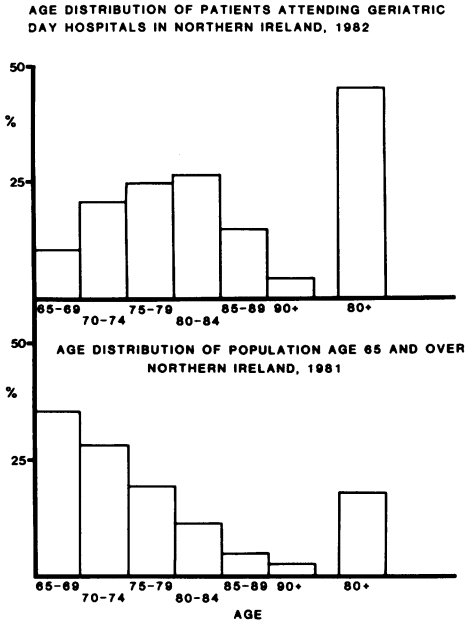


Fig 7. Age distribution of patients attending geriatric day hospitals in Northern Ireland compared with age distribution of total population of Northern Ireland aged 65 and over. [19]

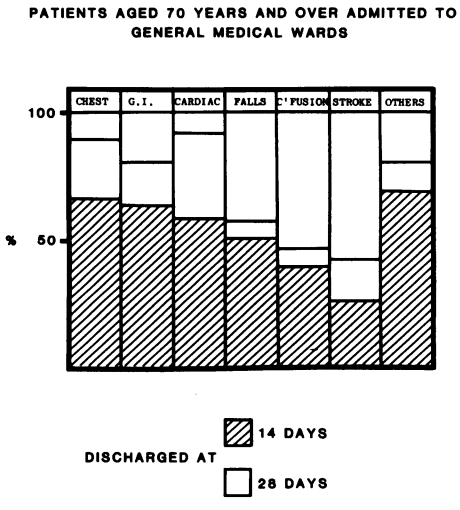


Fig 8. Discharge of patients aged 70 years and over admitted to general wards of the Royal Victoria Hospital in relation to main diagnosis on admission. Columns represent per cent discharged 14 and 28 days after admission. [20]

to acute medical wards in the Royal Victoria Hospital[20] and has identified the conditions which are associated with delayed discharge (Fig 8). Of the admission diagnoses, three resulted in a considerable delay in discharge with fewer than half of those admitted being discharged within 28 days. These were falls, confusion and stroke — clearly areas in which major problems occur in elderly people and where further knowledge would be of great importance.

## STROKE

Stroke has traditionally been an area of interest to geriatric units and nowhere more so than in Belfast. Dr Ken Fullerton has carried out a prospective study of over 200 patients with stroke to try to identify those factors which are important in prognosis.[21] Stroke is commonest in old people (Fig 9). Prognosis from stroke is poor. Six months after the stroke 45% of patients have died and only 18% have recovered completely (Fig 10). The patients who survive but do not recover total independence are particularly important because of the burden of disability this causes. Dr Fullerton has identified six factors which appear to be related to outcome from stroke (Table II) and has devised a prognostic index which allows patients, at the time of onset of stroke, to be placed in a prognostic category. In this way patients who require particular attention can be identified. The prognostic index should also be of value in further trials of management of stroke.

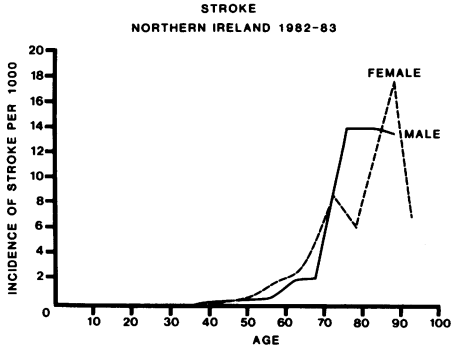


Fig 9. Annual incidence (per 1,000 population) of stroke in the Southern Area of Northern Ireland in males and females in relation to age. [21]

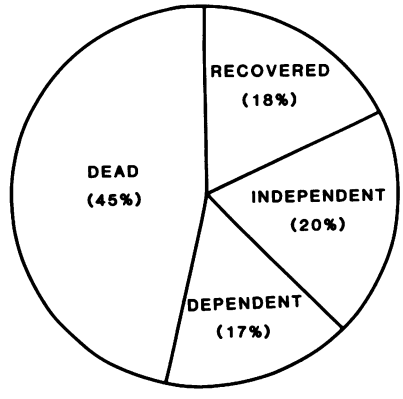


Fig 10. Outcome of 205 stroke patients six months after the onset of the stroke. [21]

TABLE II

*Factors related to outcome from stroke*[21]

| |
|---|
| Level of consciousness |
| Arm power |
| Leg function |
| Albert's Test score |
| Mental score |
| ECG changes |

## FALLS

As well as identifying those areas which may be useful to pursue further, it is also valuable, but much less dramatic, to identify measures which, although widely advocated, turn out to be of little value. In the last decade it has been suggested that some neurological symptoms in elderly patients, including falls and mental disturbance, may be related to disorders of cardiac rhythm. Frequent but transient arrhythmias may reduce cardiac output and the blood flow in the cerebral circulation and hence cause damaging effects on brain function. Dr Ian Taylor carried out a study of cardiac arrhythmias in elderly people with a number of conditions, including these 'funny turns' of which so many complain.[22] Unlike previous investigators he also studied cardiac rhythm in elderly people without symptoms. Like others he found that cardiac arrhythmias are common in elderly people with 'funny turns' but that they are not more common than in those who did not have these symptoms (Table III). Nor did any of the arrhythmias cause symptoms at the time of the investigation. Thus, while the cause of frequent falls and other 'funny turns' in elderly people has not been identified, at least the idea that disturbance of cardiac rhythm is a major cause does not need to be pursued further.

TABLE III

*Disorders of cardiac rhythm in elderly patients with 'funny turns' and asymptomatic controls*[22]

| *Type of arrhythmia* | *Patients with 'funny turns'* | *Controls* |
|---|---|---|
| | % | % |
| 1 | 29 | 9 |
| 2 | 53 | 59 |
| 3 | 0 | 9 |
| 4 | 9 | 12 |
| 5 | 12 | 18 |

## FRACTURES

One of the important complications of falls in old people is fracture, particularly fracture of the proximal femur. Dr Hugh Taggart and Dr Tim Beringer have been interested in this problem.[23] There is a close relationship between the incidence of fracture and that of age (Fig 11). Many elderly people who fall and break their legs recover rapidly after appropriate surgical treatment and return to

independence without delay. Some are so disabled before their fall that independence is never regained. But there is a middle group for whom the regaining of independence is very much determined by appropriate treatment and rehabilitation. Since 1981, all the elderly patients admitted to the Belfast City Hospital with femoral neck fractures have had details of their illness entered into a computer programme in the Department of Geriatric Medicine. In general, fractures of the proximal femur affect one of two parts of the bone — the cervical region or the trochanteric region. This audit has revealed that patients with cervical fractures are younger, fitter and recover more rapidly than patients with trochanteric fractures (Table IV). Thus, it is patients with trochanteric fractures who require particular attention.

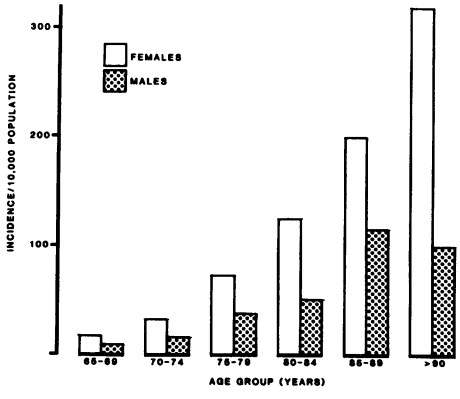


Fig 11. Annual incidence (per 10,000 population) of fracture of the proximal femur in Belfast in males and females in relation to age.[23]

TABLE IV

*Outcome of elderly people with fractured proximal femur affecting the cervical or trochanteric region of the bone*[23]

| | *Outcome* | | *Mean age (years)* | *Median length of stay (Days)* |
|---|---|---|---|---|
| | Death | 17% | 83.0 | 50.0 |
| CERVICAL | Home to residential accommodation* | 6% | 82.4 | 148.5 |
| FRACTURE | Continuing hospital care | 3% | 83.3 | 167.0 |
| (n = 87) | Return to previous environment | 74% | 78.0 | 28.5 |
| | TOTAL | 100% | 79.3 | 31.0 |
| | Death | 27% | 84.8 | 35.5 |
| TROCHANTERIC | Home to residential accommodation* | 3% | 81.0 | 126.0 |
| FRACTURE | Continuing hospital care | 6% | 88.5 | 191.5 |
| (n = 63) | Return to previous environment | 64% | 83.0 | 51.0 |
| | TOTAL | 100% | 83.7 | 49.5 |

* Patients admitted from home and discharged to residential accommodation.

## ENVIRONMENTAL TEMPERATURE

Analysis of fracture incidence in Belfast has shown that fractures are more common in winter months when temperatures are lower (Fig 12). The reason seems obvious — old people slip on icy paths, fall and break their legs. The problem with this explanation is that 85% of the fractures occurred indoors. In Dr Fullerton's study of strokes, the same relationship of stroke incidence to environmental temperature occurred (Fig 13). Thus, it appears that low temperatures have subtle effects on health, not necessarily causing hypothermia but causing other harmful effects. Other studies have shown that low temperature is associated with higher blood pressures[24] and with changes in clotting factors.[25] Raising the environmental temperature even a few degrees may result in important improvements in the health of old people.

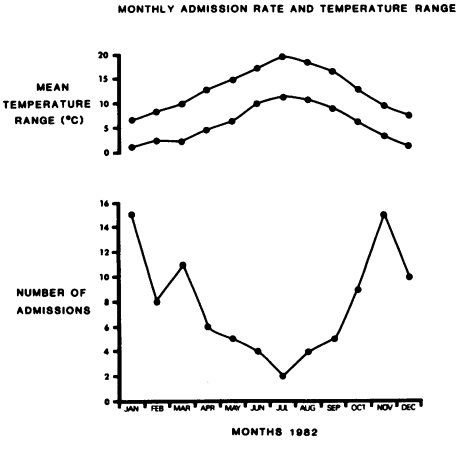


Fig 12 (left). Number of admissions for fractured proximal femur in Belfast and mean monthly maximum and minimum temperatures in 1982. [23]

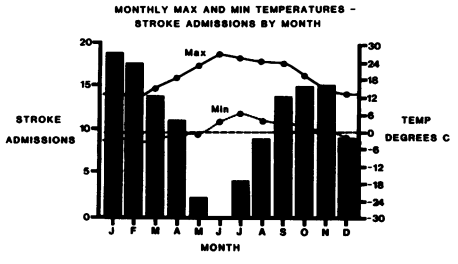


Fig 13 (above). Number of admissions for stroke in the Southern Area, Northern Ireland, and mean monthly maximum and minimum temperatures. [21]

## DEMENTIA

The remaining symptom which was associated with delayed discharge in Dr Maguire's study was confusion. Dementia is closely related to age and is most common in the over 80s. Thus there will be a great increase in the number of people with dementia in the next few decades (Table V). Epidemiological studies in Newcastle-upon-Tyne have shown a change in the pattern of survival of patients with senile dementia between the 1940s and 1970s.[26] Mortality has

TABLE V (a)

*Age-related prevalence of dementia*

| *Age* | *Prevalence* |
|---|---|
| 65 – 69 years | 2.3% |
| 70 – 74 years | 2.9% |
| 75 – 79 years | 5.5% |
| 80 years and over | 22.0% |

TABLE V (b)

*Predicted number of people with dementia in Northern Ireland, showing effect of increasing number of very old people*

| | *Population aged 65+* | *% change since 1985* | *People with dementia* | *% change since 1985* |
|---|---|---|---|---|
| 1985 | 179,000 | — | 11,758 | — |
| 1990 | 181,000 | +1.1 | 12,391 | +5.4 |
| 1995 | 182,000 | +1.7 | 13,289 | +13.0 |
| 2000 | 178,000 | −0.5 | 12,861 | +9.4 |
| 2005 | 177,000 | −1.1 | 13,017 | +10.7 |
| 2010 | 183,000 | +2.2 | 13,103 | +11.4 |
| 2015 | 192,000 | +7.3 | 13,366 | +13.7 |

decreased but the number of those who are inpatients has increased as has the number of those in residential care. Thus, although physical disability in old age may be less prevalent, mental disability in old age is an increasing problem. It seems that, as with the decline in infectious disease which resulted in the appearance of physically disabling conditions, so a decline in physical disability in old age may reveal the major problem of senile dementia. Dementia is not a condition which produces a rapidly fatal outcome, but the burden on families, on social services and on the hospital service caused by dementia is considerable and will increase unless we can gain some further insights into its cause and cure.

## POSTPONEMENT OF DISABILITY

Is there any evidence that the burden of disability in old age is declining or being postponed into more advanced age? The recent decline in mortality from coronary disease and stroke may be evidence of this.[27] It could be argued that, if mortality is all that is measured, then medicine may in fact be creating survivors who add to the burden of cardiac or neurological disability in old age. It is likely, however, that in these conditions morbidity and mortality are related and that incidence, not just case fatality, is declining.

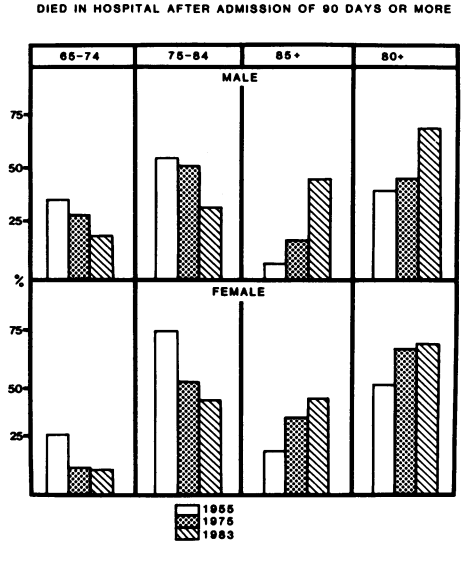


Fig 14. Age at admission of elderly patients to the Geriatric Medical Unit, Belfast City Hospital, for continuing care (defined as those who died in hospital after an admission of 90 days or more) in 1955, 1975 and 1983.

The Geriatric Medical Unit of the Belfast City Hospital has kept detailed records since it first came into operation in 1948. Using these records the age of admission of patients requiring long-term hospital care has been assessed over a period of 28 years. These patients have been defined as those who died in hospital after an admission of at least 90 days. Between 1955 and 1983 there has been a shift in the age of admission of both men and women towards the older age groups (Fig 14). In particular, there has been a steady increase in the age of admission of women and a more recent increase among men. This is evidence that disability in old age is being postponed. Whether the postponement of disability is occurring more rapidly than the increase in life expectancy is not clear. If this is occurring, the time of terminal disability in old age will be shortened, Further analysis is required to answer this question.

## CONCLUSIONS

One of the most important features of ageing in the 80s is the great increase in the number of very old people — in their 80s and over. This is due not only to increased survival of younger people into old age, but also to a reduction in the mortality of the very old. In old age decreased mortality does not necessarily imply improvement in the health and quality of life of the survivors. The challenge

is not only to reduce mortality in old age but also to reduce the period of disability and dependency which is the fate of so many old people in the last phase of their lives. Although the age of onset of terminal dependency may have been postponed in the last thirty years, the length of time spent in continuing care has not decreased. Unless the prevalence of disability in old age can be reduced more rapidly than the increase in the number of people entering the later years, the demand for high dependency care will continue to rise.

An approach to reducing disability in the elderly is to identify the most important reasons for prolonged hospital care, and to study these conditions in detail to identify areas where improvements may occur. Such an approach has had some success when applied to the problems of stroke, falls and fractures in old age. Dementia remains one of the major unsolved problems in the elderly and is likely to assume even greater importance as a cause of disability and dependence as the population continues to age. Nevertheless, as individuals, 80-year-olds in the 1980s have better health than ever before, are more likely to respond to treatment if they develop an acute illness and are less likely to develop a chronic disease. The 80s in the 1980s have a good chance of being the 90s in the 1990s and centenarians in the next millenium. We must redouble our efforts to ensure that this will be a welcome development.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 122 – 126, October 1985.*

# Medical problems at Belsen Concentration Camp (1945)

J T Lewis

With an introduction by H G Calwell,
Honorary Archivist, Royal Victoria Hospital

## INTRODUCTION

*Among the documents deposited in the archives of the Royal Victoria Hospital is the autographed typescript of a lecture bearing the above title delivered to the Ulster Medical Society on 1st November 1945 by the late Joseph Tegart Lewis (1898-1969), who was connected with the Royal during the whole of his professional life. The lecture has never been published.*

*He served the hospital as resident medical officer, resident clinical pathologist and medical registrar. He became an honorary assistant physician in 1929, an honorary physician in 1946, and with the inception of the National Health Service he became a consultant physician. He retired in 1963.*

*In 1940 he joined the Royal Army Medical Corps, served with the 8th Army in the desert and was taken prisoner on the fall of Tobruk; after two years' captivity he was repatriated in 1943 under the Geneva Convention regarding medical personnel. He returned to military service as Lieutenant-Colonel in charge of the medical division of a General Hospital, landed in France in 1944 and took part in the Allied advance into Germany which led to the surrender of the German Army in 1945.*

*The fortieth anniversary of the Nazi defeat and surrender on 10th May 1945 has been celebrated in this present year 1985, and the word Belsen has again rung around the world because of the controversial visit of the President of the United States of America to a German war cemetery containing the graves of Hitler's Storm Troops, who were the agents of many atrocities committed against Jews in Belsen and other concentration camps. At the time of the Nazi surrender, the General Hospital in which Dr Lewis was serving was in the neighbourhood of Belsen, and it was sent into the camp to provide medical service for those imprisoned there. What he and his colleagues saw and did there is related in his lecture. The text of the lecture runs to over 80,000 words. It has therefore been necessary to abbreviate it severely and to edit it according to the space available in the* Journal. *It is hoped that the reader is left with an adequate picture of what Dr Lewis called 'the Horror Camp'.*

*HGC*

Abbreviated from the typescript of a lecture delivered to the Ulster Medical Society on 1st November 1945.

J T Lewis, MD, FRCP. (1898-1969).

Correspondence to: Dr H G Calwell, Hon. Archivist, Royal Victoria Hospital, Belfast BT12 6BA.

When the unit to which I was attached arrived at Belsen after the German surrender, preliminary clearing of the camp had already been done. This was soon completed, and we were present at the official 'burning down' of the Horror Camp.

With the completion of the transfer of patients to the hospital set up in the nearby German barrack settlement, it was found that about 12,000 were in urgent need of medical attention if they were to survive. Two general hospitals were given this task. Our unit, designed and staffed for 1,200 patients, took over about 8,000. We allotted one British medical officer to every 650 patients and a nursing sister to every 150. In addition, there were medical students and Swiss, Italian and German doctors, the last being prisoners-of-war. To these were added doctors who were themselves prisoners in Belsen. The Division of which I had charge took over the care of about 4,500 patients.

I will now pick out the most outstanding groups of cases:-

## STARVATION

This was universal. It varied considerably in degree; a minority of the internees showed a surprisingly good state of nutrition, but many thousands had reached a state of exhaustion and emaciation impossible to believe in a civilised community. The advanced cases presented a terrible spectacle — pitiful skeletons were crawling around looking for scraps and searching in swill bins. In some cases their superficial bones had burst through the skin.

We tried the following methods of treatment according to whether the patient was able to swallow or not.

For those unable to swallow:-

(1) Casein hydrolysate with glucose-vitamin solution given intravenously. This was not a great success. The amount given daily had to be about two litres which the circulation could not stand, and patients frequently collapsed and died. At post-mortem examination it was found that the adult heart had atrophied to about the size of the heart of a ten-year-old child, and the aorta was about the size of a pencil. Hydrolysate treatment was abandoned.

(2) Double-strength plasma or serum was given intravenously; the amount was only half a litre which was sufficient to maintain nitrogen balance. Glucose was also given.

For those able to swallow:-

(1) Casein hydrolysate orally — this was very nauseating, and it was given up.

(2) Unsweetened condensed milk diluted to 1 in 4, or skim milk powder in water, 3 oz feeds frequently. This was the most satisfactory method. In the absence of any complicating disease the patients improved rapidly.

I should next like to mention two diseases closely associated with and really part of the starvation syndrome:-

## DIARRHOEA

This was present in all severe starvation cases. There appeared to be four possible causes:

(1) A dysenteric infection: Only a few stools could be examined; true dysentery was not common.

(2) Intestinal tuberculosis was a common cause as many patients with diarrhoea had manifest pulmonary tuberculosis.

(3) Vitamin deficiency of the pellagroid type: In a group of patients with no evidence of tuberculosis treated only with nicotinic acid about 60% responded rapidly.

(4) Pure starvation: We placed in this group patients who did not appear to be tuberculous or dysenteric and who did not respond to vitamin therapy. In those who died, post-mortem examination showed the large bowel much thinned and almost transparent, the musculature being completely wasted. The mucosa was ulcerated.

## FAMINE OR HUNGER OEDEMA

This was present in all our severe starvation cases and varied from moderate pitting of the shins to massive oedema with ascites and pleural effusion. Nephrotic and cardiac oedema were uncommon. The idea generally held that famine oedema is the result of hypoproteinaemia did not seem to be the complete answer as there were patients with low serum protein and little oedema, and vice versa. Vitamin deficiency, 'unknown toxins', etc., all had their advocates. Unfortunately, the oedema fluid was not investigated. In most of the cases where post-mortem examination was done, large blebs of oedema fluid were present on the pericardial sac.

Again our weapon was feeding, and often daily transfusions of double strength plasma or blood caused a rapid decrease in the oedema. Other patients responded to oral feeding with diluted milk but in some the oedema persisted in spite of improved nutrition. A trial with Salyrgan gave good results, and it was found that removal of the oedema by diuresis often produced a desire to eat, and marked improvement followed.

## ANAEMIA

The average haemoglobin was around 50%, although patients looked intensely anaemic because of their pallor, which was probably due to a combination of vascular spasm and dehydration. In the few cases examined by sternal puncture, the marrow looked normal. The sternum was often soft and cheesy. Iron was always given, but this may not have been necessary. In cases where the anaemia did not improve one always thought of tuberculosis, and one was right in most instances.

## TYPHUS

When we arrived at Belsen, the acute epidemic was dying down, thanks to our predecessors' work in cleansing and disinfecting the patients. Sporadic cases kept occurring, and in some the diagnosis was very difficult. The rash was often scanty and atypical, and the Weil-Felix almost always positive in high dilution which might only indicate previous typhus. The final conclusion was that probably many of these patients were not suffering from typhus, but it was regarded as safer to regard them as such.

We encountered a large series of patients with post-typhus complications, most of which were quite new to us. The commonest were thrombophlebitis, gangrene of the feet, and meningitis (a benign form with a good prognosis, the cerebrospinal fluid showing a marked increase in protein). The differential diagnosis was always

from tuberculous meningitis. The continental doctors emphasised that typhus was common, and many of the patients, when convalescent, complained of severe attacks of chest pain. We had, of course, no electrocardiograph to investigate these cases.

## TUBERCULOSIS

Perhaps I should have mentioned this disease first because it was by far the greatest cause of death in Belsen. It was not easy to get an idea of the proportion of patients suffering from tuberculosis because our X-ray and laboratory facilities were scanty. However, in one series of 1,575 suspected cases we found over 30% with extensive and often bilateral lesions. We came to the conclusion that 25% of all the patients in Belsen were probably suffering from acute tuberculosis. All this is not surprising when one considers the degree of malnutrition and the appalling conditions in the original huts where the prisoners were packed, not only in one tight layer but often in several layers, with the dead forming a mattress for the living.

All the usual types and distribution of lesions were found, including many diffuse miliary cases, and a high proportion of patients had acute pericarditis. Tuberculous laryngitis was common and increased the patient's sufferings enormously. Glandular tuberculosis did not appear to be common. Pleural effusions were very common, being present in about half of the patients with tuberculosis. Peritonitis was relatively rare, but it was sometimes difficult to decide whether a patient with active tuberculosis, starvation and generalised oedema with ascites, had peritonitis or not. There were very few cases of meningitis.

## VITAMIN DEFICIENCY

It was at first surprising that we did not see well-marked cases of vitamin deficiency, but raw turnips and raw potatoes were eaten when they could be obtained, and this probably accounted for the complete absence of vitamin B-complex deficiency. I saw one boy with what appeared to be pellagra affecting the skin, the mouth, the intestine and his mental state. He responded well to nicotinic acid.

## MINOR COMPLAINTS OF INTEREST

(1) A condition suggesting acute cholecystitis was sufficiently common as to attract attention. We had previously observed at post-mortem examinations on patients dying from tuberculosis or other diseases that the gallbladder was frequently abnormal.

(2) 'Belsen Fever': We gave this name to a fever which we could not classify; the chief features were a swinging pyrexia lasting 2-3 weeks, enlargement of the spleen, leucopenia, no rash, negative Widal, and no abnormal organisms in blood, urine or faeces. It may have been an abnormal form of typhus, but we never came to any definite conclusion. None of the patients died.

(3) Acute upper abdominal pain: This occurred especially soon after feeding had commenced. It was no doubt the result of alimentary atony, and it subsided in a few days.

(4) Enlargement of liver and spleen: This was found quite frequently with normal blood picture and no other signs except occasional enlarged glands. We were unable to investigate these patients further.

I think I have now mentioned most of the clinical problems we met and, if the account appears confused and disconnected, this may be put down to the fact that I have compiled it from memory and from rough notes jotted down at the time. We had great difficulty in obtaining equipment, instruments, crockery and other ward utensils, and our dispensary staff did fine work in sorting out the masses of captured German drugs and giving us a sort of Belsen Pharmacopoeia.

Anything I may say will be totally inadequate to express our admiration for the work of the British Nursing Services. I am sure that, since Florence Nightingale's work in the Crimea, British Nursing Sisters have never been faced with such a task as Belsen. They had to cope with dreadful bed sores, incontinence and the tragedy of numberless deaths. Added to this were the language difficulty, the feeding, and the great tact required in dealing with nurses from other European countries. Yet in a month they had transformed the place: their work was endless and the mental strain acute, but they stuck it out to the end without complaint. Almost all the credit for what we did in Belsen is due to the Sisters and, if the story of the camp is ever written, it is hoped they will be given the high place they deserve because they have shed a lustre on British nursing which will never be forgotten.

In my Division, which had the care of approximately 4,500 cases, we were able to discharge as fit just under 2,000 patients after about two months' treatment. Sweden very generously agreed to accept our more chronic invalids who were fit to undertake the journey by rail and sea, and all our orphans. We disposed of about 1,500 in this way. At this stage we handed over to a small military unit and moved from Belsen, not without regret, for we realised that we had been privileged to see a clinical sight not easily forgotten.

*The Ulster Medical Journal, Volume 54, No. 2, p. 127, October 1985.*

# Jessie Braidwood Webster

## MA, FSA (Scot), ALA, 1909-83

## Medical Librarian, Queen's University of Belfast, 1942-1974

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Miss Webster pioneered the first regional health care library service in the United Kingdom. The report of the Medical Library Committee to the Queen's University Library Committee in 1951 records the receipt of the first annual grant from the Northern Ireland Hospitals Authority (NIHA) to supplement the library stock and make the library available to NIHA personnel. Her library, the Medical Library, was separated from the Main Library in 1954 when the University opened its Institute of Clinical Science on the Royal Victoria Hospital site. In 1973 she served on a DHSS (NI) Working Party whose recommendations provide the basis of the present regional library service which came into being just after she retired in 1974.

For five months during 1951 as the holder of an MLA Fellowship, she studied medical librarianship in the United States and made many friends there. In 1971 she travelled, under British Council auspices, to act as a specialist adviser and to report on the Medical Library at the University for Health Sciences, Yaounde, East Cameroon.

Within the United Kingdom she was active in the Library Association, serving as Honorary Secretary of the Northern Ireland Branch and as a Committee Member of the national Medical Section. As a member of the Library Association of Ireland she was a regular attender of meetings and conferences and, although retired since 1974, maintained a close interest in the profession and in 'her' library.

Jessie Webster was associated with the Ulster Medical Society, and the *Ulster Medical Journal,* for many years. She found friendship within the medical community and thus her working and her social life blended together. In her professional capacity she made herself aware of the research interests of her colleagues. She scanned the literature for relevant material, doing manually a task now largely delegated to computer data banks and local printouts.

She greatly appreciated the support and assistance of her medical friends during her long illness. In many ways they repaid her for the services which she, for so long, had rendered to them.

WDL

*The Ulster Medical Journal, Volume 54, No. 2, pp. 128 – 132, October 1985.*

# The changing interface between primary and secondary care

Julian Tudor Hart

Accepted 1st May 1985.

The way that care of the population is shared, divided, and duplicated between community generalists and hospital specialists is changing. Whereas in 1959 35% of babies were born at home, by 1983 this had fallen to less than 1%. Dr Kirk Forsythe surveyed the 412 deaths in his Belfast city practice from 1946 to 1969: less than 40% died in hospital.[1] I have surveyed the deaths in my Welsh mining village practice: from 1964-1973, of 234 deaths, 32% died in hospital and 66% at home; more recently, from 1974 to 1984, the proportion dying in hospital rose to 40% of 229 deaths, and the proportion dying at home fell to 58%. Of all deaths throughout England and Wales in 1969, only 40% died at home and 57% in hospitals or institutions.[2] Major life events, virtually all births and a rising proportion even of physiological deaths, appear to be moving inexorably from the responsibility of community generalists to that of hospital specialists.

General practitioners have lost their grip on birth and are losing it on death, but we may still imagine, in the words of the General Medical Services Committee of the British Medical Association, that we 'deal with over 90% of episodes of ill health treated by the National Health Service at only 6% of its total costs'.[3] According to Fry,[4] general practitioners refer an average of 17% of their populations to hospital specialists each year. General practitioners taking part in the 1971/72 National Morbidity Survey referred only 9% of their populations at risk, and 14% of patients consulting over one year.[5]

The General Household Survey in Great Britain found that about three times as many people attend their family doctor in any period of six weeks, as attend an outpatient department. But we know the true burden of illness for which all of us should be responsible cannot truthfully be divided into sickness episodes of equal weight, since most of them are minor and self-limiting. What really matters is the episodic but eventually cumulative loss of health represented by chronic states such as diabetes, hypertension, airways obstruction, or psychotic illness. Knowing what we do of the natural history of disease we cannot be content merely with listing the proportion of patient demands which rest with the general practitioner, and are not passed on to the hospital. In any progressive conception of the future, what really matters is the division of labour for the conservation and anticipatory care of health, our response to needs and not merely to demands.

A paper presented to the Ulster Medical Society on 14th March 1985.

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## DIVISION OF RESPONSIBILITY

The only way we can measure this division of responsibility is to look at specific conditions, and then the news is much less reassuring. When Doney[6] looked at all the known diabetics in a practice population of 20,000, he found roughly equal numbers attending their own family doctors and attending hospital outpatient departments, but over half of them were not having any medical supervision at all. For all chronic conditions, particularly where symptoms are obtrusive only in advanced disease and medical needs therefore precede patient demand, there are really three, not two levels of care: primary care by the general practice team, secondary care by the hospital team, and no medical care at all by anyone (care either never begun, or perhaps more often lapsed in disgust at its perfunctory or impersonal quality, wherever it is given). It is often assumed that this third category (no care at all) either doesn't exist, or will spontaneously disappear as civilisation advances. This was always a complacent assumption, and now that our civilisation is being moved backwards it is absurd. Our colleague Dr Sir Gerard Vaughan has recently explained, in a speech to the Pharmaceutical Association, that it costs the nation about £50 each time someone steps into an outpatient department, and £5 each time someone sees a general practitioner, but a visit to the friendly neighbourhood chemist costs the taxpayer nothing at all. 'We have a climate for change', he said, 'and the government is willing to contemplate it . . . we could see some quite rapid changes'. We could indeed.

## DIVISION OF DISEASE

The general line of thought is clear and apparently full of common sense. Medicine, we are told, can be divided into trivial disorders, which patients can deal with themselves, perhaps with some help from a chemist at their own expense; minor disorders, which can be cared for by general practitioners at relatively low cost to the state; and major disorders, which have to be referred to specialists, at a cost which seriously threatens the nation's commitment to keep bankers in the manner to which they are accustomed. Such a philosophy evidently underlay the first version of the government's limited list of drugs prescribable in the National Health Service in late 1984, which reduced the preparations available for treatment of constipation to two. There was an implicit assumption that constipation can usually be regarded as a trivial disorder suited to management by patients themselves, and prescription by a chemist.

As we all know, common sense derives from common experience. Cancer of the colon and rectum[7] is an uncommon experience for patients and government ministers, but an all too frequent experience for doctors, who see over 16,000 people die each year from this cause in the United Kingdom, second only to lung cancer as a cause of death from malignant disease. Five-year survival has risen only from 24% in 1959 to 30% in 1975, although tumours which have not yet penetrated the bowel wall have an 80–90% five-year survival. One reason for this difference between 30% actual and 85% potential five-year survival lies in the average eight to nine months' delay between onset of symptoms and surgical treatment.[8,9] Administrative action which encourages self-diagnosis and treatment by chemists for abdominal symptoms can only make these discouraging figures even worse. It is an irresponsible social act, particularly coming from a group of people who are generally very careful to avail themselves of the very latest technology in screening and anticipatory care to protect their own health.

Is the division between minor disease and major disease any easier than the division between minor disease and trivia? Students of my generation learned that there were two kinds of diabetes: the major kind, insulin-dependent, likely to cause blindness and renal failure and best left to experts, and the minor kind, a divine punishment for gluttony treated by writing repeat prescriptions for anti-diabetic agents, which presented acute difficulties only in the event of intercurrent illness. For both kinds of diabetes, what seemed to matter most was accurate management of crises; good supervision and control day after day, month after month, and year after year was regarded as an unattainable ideal for all but a minority of unusually intelligent or well-educated patients, and in any case was probably ineffective in preventing complications. That comfortable but lethal set of assumptions, tottering since retinopathy became treatable and glycosylated haemoglobin became measurable, should have been stopped dead by Hayes' and Harries' comparison of general practice and hospital outpatient care of type II (non-insulin-dependent) diabetics in Cardiff.[10] After five years, patients allocated randomly to follow-up by their own doctors had died at three times the rate of those randomly allocated to follow-up in a hospital diabetic clinic.

Diabetes, hypertension, asthma, epilepsy, alcohol dependence, and recurrent depression, to cite a few of many available examples, cannot be usefully or safely classified as minor conditions. In every case, if we wait for them to become major before taking effective action, we miss the most favourable opportunities to arrest them. Nor can they be regarded as too complex for management by community generalists. The superiority of hospital outpatient management of the Cardiff diabetics depended not on specialised skills, but on a simple but organised, regular search for retinopathy, proteinuria, and neuropathy, together with monitoring of weight and glycosylated haemoglobin, and reinforcement of patient education. If similar teamwork and organisation were generally available in primary community care, specialists at district hospital level could devote more time to the management of complex organ damage and the minority of exceptionally difficult diagnostic problems which really do require specialist training. The difficulty in general practice is structural. It lies in the continued assumption that elementary standards for care of groups will be attained simply by exhorting excellence in each individual doctor-patient encounter, rather than by recruiting ancillary staff, planning their deployment, and auditing team performance on the lines developed by the best hospital departments. The general practitioner working alone is no more capable of delivering excellent care in each one of an average 9,000 consultations a year, than a consultant working on his own would be in the same circumstances. Putting doctors into groups does not of itself change the passive, demand-oriented nature of the general practice we inherit from the past. The essential step is the creation of a team accepting some elements of forward planning related to the population at risk.

The sheer volume of health impairment in the community precludes any solution based on outreach from hospital clinics, though, until all practices develop a planned teamwork approach, this will be the solution which most progressive consultants will seek. In Glyncorrwg 2% of the population aged 20 to 64 have diabetes, 7% have a known alcohol problem, 10% have a diastolic pressure sustained at or over 100 mmHg, 16% are sufficiently obese to shorten their lives (body mass index at or over 30), 22% have substantial airways obstruction (peak expiratory flow rate less than 300), and 28% admit to regular cigarette smoking. Of course, these problems overlap. For example, 12 out of 25 adult diabetics

also needed antihypertensive drugs, with a mean pre-treatment pressure of 203/114. In one way or another, all of these health impairments need planned medical and nursing time at primary care level, if we are to avoid the organ damage that ultimately requires hospital specialist skills, and fragmentation of whole-person medicine into the disintegrated care of organs.

## THE FUTURE OF THE GENERAL PRACTICE/HOSPITAL INTERFACE

Structural change in general practice is going to come in the next couple of years, whether we like it or not. Staying as we are is no longer an option. Just as the imposition of the limited prescription list at the behest of the Treasury creates an opportunity for us to improve prescribing in the interest of better care, if we have the courage to transform it into our own initiative operated through our own machinery (for example, the editorial committee of the British National Formulary), so could the frequently postponed Government Green Paper on primary care (doubtless equally philistine in conception and ham-fisted in application) create an opportunity for a new general practice contract, related not to head-counting but to useful social performance. We still have a few months left to sort out our ideas about the kind of general practice needed to cope with health problems as they really are, in the interests of the patient rather than the Treasury, but if they don't start moving forward in our own preferred directions, we shall be pushed back into a primitive trade we thought we had left forever.

In preparing this lecture I had a look at all the outpatient referrals from our local population of 2,000 in 1981. There were 185 referrals altogether, 9% of the population at risk. About 60% of these were surgical or traumatic, few of which could or should have been managed at primary care level, with the possible exception of some of the ENT cases. There were only 25 medical and paediatric referrals during the year, 13% of all referrals. Contrary to expectation, analysis of these showed that either shared care with an agreed division of labour, or rapid return to primary care after useful investigation and/or advice, were the rule rather than the exception. The minority of consultants who will not consult is as obtrusive to general practitioners as the minority of family doctors unwilling to practice clinical medicine is to consultants. Careful reading of correspondence from both sides confirms that, though both problems are real, they can be and in most cases are being overcome, and are not a valid excuse for not trying to improve co-operation between primary and secondary medical teams. Medical, paediatric, and psychiatric referrals in Glyncorrwg are now between one half and one tenth of average national rates. Wherever practices employ and/or attach a full team of ancillary staff, and plan the follow-up of chronic disorders in their practice population, this downward trend in referrals will continue.

Consultant internists will face diminishing pressure from outpatients' referrals, in the quantity if not the quality of problems referred. As inflated training grades hopefully fall to the size required to maintain consultant numbers (though at a higher level than we have now), consultants should be able to develop their work in new directions. Some of this will be better inpatient care of advanced organ damage, but just as the way forward for general practitioners is to plan their work in relation to the needs of their whole registered populations, hospital specialists might be more effective if they took themselves more seriously as community clinicians, planning their work in relation to the needs of their catchment area, in association with primary care generalists.

In 1985 we stand, as never before, on the brink of an unknown future. In all the years since 1945, we knew that next year would simply be plus or minus 5% of

the last: now we are stepping out into the void, into a place where no man and no nation has ever been before. A political and social realignment is taking place on a scale not seen since the 19th Century, in the world's oldest and most fully developed industrial society, for which no valid international or historical models exist. Medical care has in the past been a socially stabilising force, with elements of a cash-free economy, organised for collective needs rather than private gain. This stabilising function, and this experience of a natural and relatively successful collective economy, could be of critical importance in developing a society that is no longer self-destructive. If we want a medical future that works, thoughtful hospital specialists and community generalists will have to stop waiting upon events, and get together with the populations they serve to design and popularise it.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 133 - 139, October 1985.

# An automated blood culture system: the detection of anaerobic bacteria using a Malthus Microbiological Growth Analyser

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Accepted 24th July 1985.


## SUMMARY

*The Malthus Microbiological Growth Analyser has proved to be sensitive in detecting conductivity changes due to anaerobic metabolism in a number of widely used blood culture media. Freshly prepared cooked meat media and Thiol medium yielded the greatest gross conductivity changes, and were more sensitive of anaerobic metabolism than other media. Failure of the instrument to detect anaerobic metabolism was a problem particularly associated with growth in the thioglycollate medium. False positive detections of growth were attributed to a number of factors including electrode instability (6.0%) and bacterial contamination (8.75%).*


## INTRODUCTION

The early detection of microbial growth in blood culture media, and antibiotic sensitivity testing of the detected organism, is of great value in the management of septicaemic patients. However, conventional methods by frequent subculture are slow and time-consuming, and place a heavy workload on laboratory staff. Frequent subculture of conventional bottles also increases the risk of medium contamination and may render results difficult to interpret. These factors suggest the potential value of an automated system for detecting microbial growth in blood cultures.

A number of different approaches have been developed to accelerate the detection of microbial growth in blood cultures. These techniques have been based on a number of different physical detection methods including radiometry [1] (Bactec), impedance [2] (Bactometer), microcalorimetry,[3] lysis filtration and centrifugation methods.[4] Among those instruments introduced recently which detect microbial metabolism is the Malthus 112L. Boynes, Comrie and Prain [5] reported the use of the system and have suggested that the type of medium used is most important when detecting changes in electrical conductivity.

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Anaerobic bacteria contribute a small but significant percentage of blood culture isolates. This study aims to show the conductance changes in different blood culture media developed for the isolation of obligate anaerobic bacteria.[7, 8, 9] Although anaerobic bacteria comprise only 6 – 8% of blood culture isolates, in most series, the media required for their isolation are often adopted with the aim of combining good rapid isolation of obligate anaerobes, facultative organisms and obligate aerobes. Thus the investigation reported here has studied those media which will enhance isolation of anaerobic bacteria, and are often incorporated in a 2- or 3-bottle blood culture media isolation regimen.

## MATERIALS AND METHODS

*Organisms*

The following stock cultures were used: *Clostridium perfringens* NCTC 8237, *Clostridium difficile* NCTC 11206, *Bacteroides fragilis* NCTC 9343, *Bacteroides fragilis* NCTC 10584, *Fusobacterium necrogenes* NCTC 10723 and three anaerobic cocci, NCTC 9803, 9811 and 9814. In addition, three current clinical isolates were examined in the system: *Propionobacterium spp.*, an anaerobic coccus, and a non-toxigenic strain of *Clostridium perfringens.*

*Media*

The media used in this study were thioglycollate broth (THG, Oxoid), thiol broth (THIOL; Difco), brain heart infusion broth (BHI; Gibco-Biocult), rehydrated cooked meat medium (BBL; Becton Dickinson); fresh cooked meat medium (FCMM) and fresh cooked meat medium plus agar (0.1% w/v) (FCMM + A). The media were prepared according to the manufacturers' recommendations with supplements as previously described.[9] BBL was reconstituted using 3 gm per 80 ml distilled water instead of the recommended 10 gm. FCMM and FCMM + A were prepared with 14 gm moist weight of meat made up to 80 ml with broth. All blood culture media were dispensed in 80 ml volumes into 100 ml Malthus blood culture bottles. After autoclaving at 121°C for 15 minutes with the bottle tops loose, the tops were tightened during cooling.

*Solid culture media*

Tryptone Soya Agar (TSA, Oxoid Ltd) was supplemented with L-cysteine hydrochloride (0.05% w/v), yeast extract (0.01% w/v) and 5% horse blood. All media were prepared just prior to use and autoclaved for 15 minutes at 121°C.

*Inoculum preparation and enumeration of bacteria*

To obtain a small enough inoculum similar to that commonly found in infected blood, a 48-hour growth on TSA plates was harvested into 9 ml of sterile saline to give a slightly turbid suspension; further dilutions were made to yield 1 – 100 colony-forming units per ml (cfu/ml). Five different inoculum dilutions for each organism were used.

Each of five volumes of transfusion blood were inoculated with one of five different dilutions of the organism. One ml of diluted inoculum was added to 49 ml of blood.

The numbers of cfu/ml in the original inoculum suspensions were counted using a spread plate method.

*The Malthus system*

The Malthus Microbiological Growth Analyser 112L consists of four waterbaths, each housing 28 blood culture bottles linked to an Exorcet 100 computer. The computer is programmed to detect changes in electrical conductivity. Each bottle contains two electrodes on a ceramic strip which can be connected to the analyser. The analyser automatically measures the electrical conductivity of the contents of each bottle, scanning each individual cell every 30 minutes. The data from each cell is stored on a floppy disk in the Exorcet computer, the capacity of which is sufficient to hold information from 128 cells for a maximum of nine days. Once the computer detects a significant change in electrical conductivity, it displays this as a detection time on a visual display unit.

*Inoculation of Malthus cell*

One ml of 2.5% sterile saponin was added by syringe to each Malthus culture bottle before addition of blood. The bottles, with added saponin, were all pre-incubated at 37°C in the water baths. Five ml of inoculated blood were added into each bottle. After inoculation the bottles were immediately placed back in the water bath and connected to the Exorcet computer.

*Detection of change in conductivity: routine procedure*

All detection times for each cell were noted and subcultures were made on TSA plates as soon as possible after detection by the instrument. Subcultures were made by passing a sterile Pasteur pipette through the inoculation port and removing a drop of the liquid media. All bottles were subcultured on to TSA at the completion of each experiment. Duplicate plates were incubated aerobically and anaerobically for 48 – 72 hours and examined for bacterial growth.

## RESULTS

*Conductivity change*

(i) *Uninoculated blood culture media.* All six media evaluated were within the range of conductivity (10,000 – 1,000 micro-siemens) set by Malthus Instruments. Detection times appeared in four out of 32 bottles containing medium only. Electrode instability accounted for two of the four detections; these erratic changes in conductance could not be confused with changes induced by growth. The remaining two cells produced false detections because of a gradual downward drift in the base line; in both cases drifts occurred in FCCM + A medium.

(ii) *Blood culture media with added lysed blood.* Altogether 56 bottles were tested with media and lysed blood. Twenty-three on incubation yielded changes in conductivity which resulted in an instrument indication of detection. Five of the total were contaminated with *Staphylococcus spp.* The remaining 18 bottles were false-positive detections of bacterial growth.

Eight (44%) of the false detection times were due to an upward or downward drift in the base lines, three were due to electrode instability and seven (39%) were attributed to various factors which were likely to be excluded with experience. Only five false detections could possibly be misinterpreted as microbial growth when the graphical representation was examined.

(iii) *Inoculated blood culture media.* The detection times of eleven stock cultures using minimal inocula in the six media are shown in the Table. From this data FCMM + A appeared to give the best performance; all 11 organisms were detected. FCMM produced similar results, but one of the anaerobic cocci was not detected; in BBL the *Proprionobacterium* was not detected; in THIOL, two anaerobic cocci were not detected, and in BHI four were not detected. THG gave the worst performance and only three bacteria were detected.

TABLE

*Detection times of 11 obligate anaerobic bacteria in six culture media using simulated blood cultures*

| | *Threshold inoculum levels allowing detection* | *DETECTION TIME (hours) IN DIFFERENT MEDIA* | | | | | |
|---|---|---|---|---|---|---|---|
| *Organisms* | *Inoculum* (cfu/ml) | *THIOL* | *BBL* | *THG* | *BHI* | *FCMM* | *FCMM + A* |
| *C perfringens* NCTC 8237 | 1 | 36 | 11 | 14 | 27.5 | 8.0 | 16.0 |
| *C perfringens* clinical isolate | 2 | 17 | 12.5 | ND/NG | 27.0 | 18.0 | 10.5 |
| *C difficile* NCTC 11206 | 10 | 33.5 | 42.5 | ND/NG | 16.5 (2) | 17.0 | 18.0 |
| *B fragilis* NCTC 10584 | 18 | 30.0 | 39.0 | (1) | 36.5 | 21.5 | 19.0 |
| *B fragilis* NCTC 9343 | 100 | 20.5 | 6.5 | ND/NG | 13.0 | 19.5 | 59.0 |
| *Anaerobic cocci* | | | | | | | |
| NCTC 9811 | 1 | ND/NG | 55.5 | ND/NG | ND/NG | 13.7 | 32.0 |
| NCTC 9803 | 2 | 30.0 | 21.0 | 45.0 | (1) | (1) | 86.5 |
| NCTC 9814 | 6 | (1) | 54.0 | (1) | (1) | 25.5 | 26.5 |
| Anaerobic coccus clinical isolate | 100 | 91.0 | 40.5 | ND/NG | 26.0 | 23.5 | 43.0 |
| *Fusobacterium necrogenes* NCTC 10723 | 6 | 18.5 | 13.5 | 28.0 | 33.0 | 13.0 | 17.5 |
| *Proprionobacterium spp* | 113 | 110.5 | ND/NG | ND/NG | ND/NG | 82.0 | 81.5 |

*NOTES* (1) No Malthus detection despite growth on subculture.
(2) Malthus detection unsubstantiated by subculture.

Media examined were THIOL (Difco), BBL (BBL cooked meat medium), THG (Brewers thioglycollate medium), BHI (brain heart infusion medium), FCMM (fresh cooked meat medium) and FCMM + A (fresh cooked meat medium + agar).

ND/NG (No instrument detection, No growth on final subculture).

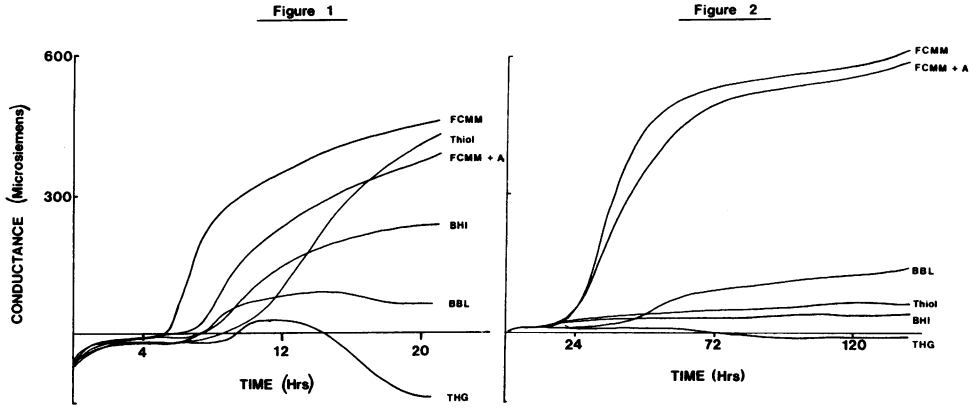
### *Recovery of anaerobic bacteria from six blood culture media*

All organisms were recovered from FCMM + A and FCMM at a minimal inoculum level; 10 were recovered from THIOL, nine were recovered from both BBL and BHI; only five organisms were recovered on final subculture from THG. The relationship between growth on subculture and changes in conductivity

resulting in detection by the system were excellent using FCMM + A. Thiol and FCMM were in agreement in all but one bottle for each media; this displayed growth on subculture without an accompanying detection by the instrument. In BBL only one detection time appeared when there was no growth; with the other 10 organisms there was a close relationship between detection time and growth on subculture. In BHI broth, with seven out of the 11 organisms tested, there was a similar close relationship. THG did not support good conductance changes when minimal inocula were used, and detection in two cells did not take place when there was evident growth on subculture.

*The effect of bacterial metabolism on conductivity changes in the six media*

In general the 11 different anaerobes produced the greatest conductivity changes in FCCM and FCCM + A media. Thiol produced changes that were only slightly lower. The conductivity changes generated by the 11 organisms in both BHI and BBL media were similar and generally lower than that of FCMM + A, FCCM and Thiol. THG supported little conductivity change for any of the organisms.




Figs 1 and 2. Conductivity changes produced in six simulated blood culture media containing minimal inocula in blood of (1) *Clostridium perfringens* NCTC 8237, 60 cfu/ml. (2) an anaerobic coccus NCTC 9814, 6 cfu/ml. Graphs are based on instrument readings taken every 30 minutes. Media used were: FCMM (= fresh cooked meat medium); FCMM + A (= fresh cooked meat medium plus 0.1% agar); Thiol (= thiol broth); BHI (= brain heart infusion); BBL (= rehydrated cooked meat medium); THG (= thioglycollate broth).

Figure 1 (*Clostridium perfringens,* NCTC 8237) and Figure 2 (an anaerobic coccus, NCTC 9814) demonstrate the differing conductivity changes due to metabolism of two bacteria on a variety of media. These figures highlight the need for a medium which produces relatively large changes in conductivity. Especially with *Clostridium perfringens,* Thiol, BHI and THG media did not support detection by conductivity changes at minimal inocula levels. For both organisms, FCCM and FCCM + A produced large changes in conductivity.

Low initial levels of inocula prolonged detection time and decreased resulting conductivity changes. This occurred with all organisms and in all six media. In FCCM + A and FCMM the decrease in conductivity was not significantly large enough for bacterial detection to be missed with decreasing inoculum levels, but in BBL and BHI media, the effect of small inocula could cause large decreases in the changes of conductivity.

## DISCUSSION

The media selected for study are widely used in blood culture systems, and are often incorporated especially for their ability to support the growth of anaerobes.[8] When judged by the detection of growth by routine subculture, cooked meat media and Thiol medium have been shown to have advantages in the range and speed of recovery of anaerobic bacteria.[9]

Successful use of the Malthus system depends on changes in conductivity induced by microbial metabolism of the available substrates. Boynes et al[5] have shown that the magnitude of conductivity change depends on the type of medium used. Our results confirm this and show that freshly prepared cooked meat media yielded the greatest gross conductivity changes. Anaerobic growth induced somewhat smaller conductivity changes in Thiol medium and substantially smaller changes in BBL, BHI and THG. In general, those media reported to be of value in anaerobic detection by conventional means seem to be the most desirable for use in anaerobic detection using the Malthus system. Cooked meat media and Thiol are the most useful and THG the least useful substrate.

The efficacy of different media in such a system should also be judged on a number of false positive and false negative alerts to detection which the instrument records. We have demonstrated with a range of anaerobic bacteria that with those media tested, excepting THG, the growth of anaerobic bacteria produces conductivity changes which are detected. Those delays in detection which we have noted in a few instances are not due to any insensitivity of the electrode detection system but to limitations of the detection programme.

False positive detection has provided a greater problem. However, at a technological level our recorded rate of false positive detections due to electrode instability of 5.4% is a confirmation of improvements made to the system since the published observations of Brown et al (1984).[6] Bottles with electrodes should in any case be tested on the analyser or by a cell-tester before distribution to wards. This will now be a practicable proposition. Increased familiarity with the instrument over a six-month period has emphasised the importance of controlling water bath levels and temperatures, careful electrode cleaning, and rapid and efficient red cell lysis. False positive detections arising from failure in these areas can be overcome only by awareness and subsequent good management.

We wish to acknowledge the help of Mrs Cecilia McIlhatton, Miss June Straghan and Miss Gillian Newberry in preparation of the text. Our thanks are due to Professor A M Emmerson, Professor of Bacteriology, Queen's University, Belfast, for his helpful and constructive criticism of the text.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 140 – 147, October 1985.*

# Clinical presentation of coeliac disease in adult gastroenterological practice

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Accepted 5th August 1985.


## SUMMARY

*Clinical features, complications and results of investigations are analysed in 50 patients diagnosed by jejunal biopsy as having coeliac disease at the Adult Gastroenterology Unit, Royal Victoria Hospital, Belfast, between 1969 and 1983. Only one patient was entirely asymptomatic, but 22% had no disturbance of bowel habit, and 50% had not lost weight. There were relatively few physical abnormalities on clinical examination. Screening tests using standard haematological and biochemical methods were positive only in between 8% and 52% of patients. More specific tests for malabsorption were positive in between 54% and 84% of patients. Jejunal biopsy remains the definitive procedure to identify patients with coeliac disease.*


## INTRODUCTION

Only in the past 30 years has 'idiopathic steatorrhoea' or 'non-tropical sprue' been accepted to be the adult variety of coeliac disease. The gluten-free diet was first used to treat adults with this condition in 1952,[1] and it is current practice that this dietary modification is recommended 'for life' to ensure continued clinical remission. It is clearly vital, therefore, that an accurate diagnosis of the disorder is made. Crosby capsule biopsy of the jejunum combined with an assessment of clinical and histological response to gluten withdrawal has become accepted as the essential approach to diagnosis. The clinical features which warrant this procedure and the role of screening blood tests and dynamic studies of absorptive function are not so well defined.

We have examined the case records of 50 consecutive patients diagnosed as having coeliac disease in the Adult Gastroenterology Unit, Royal Victoria Hospital, Belfast, between 1969 and 1983. We describe the presenting symptoms and signs of these patients and the results of their initial screening investigations.

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## METHODS

A retrospective survey in the Medical Records Department, Royal Victoria Hospital, Belfast, identified 50 patients who were investigated and diagnosed as having coeliac disease in the Gastroenterology Unit of that hospital between 1969 and 1983.

Patients were accepted into the study if they had histological evidence of severe partial villous atrophy or subtotal villous atrophy on jejunal biopsy and if a good clinical response to gluten withdrawal had been observed. For each patient, details of presenting symptoms and signs, screening blood tests and malabsorption studies were recorded. Body weight at presentation and at outpatient review after institution of the gluten-free diet was also noted. Complicating illness or associated disease in these patients were documented.

*Interpretation of tests for malabsorption*

An abnormal faecal fat collection was recorded if a patient excreted more than 5g fat daily over a three-day period while on a 50g fat diet. In the fat breath test, breath radioactivity was measured at five, six and seven hours after administration of an oral dose of 5 μCi $C^{14}$-labelled glyceryl tripalmitate, and fat malabsorption was diagnosed if the maximum concentration of $^{14}C$ per millimole $CO_2$ in expired air was less than $20 \times 10^{-14}$%. The D-xylose test was performed with a 25g dose in eight patients, and impaired xylose absorption was recorded if less than 17% of the oral dose was collected in a five-hour urine collection; a 5g dose was used in 33 patients and absorption considered to be impaired if less than 23% of the oral dose was collected in a five-hour urine collection. A glucose tolerance test was reported as showing a flat response due to malabsorption if the maximum blood glucose rise after a 50g oral dose was less than 2.2 mmol/l.

## RESULTS

The age of patients at presentation to hospital for assessment was widely varied. There were 16 men whose ages ranged from 15 to 57 years (median, 30 years) and 34 women whose ages ranged from 13 to 71 years (median, 30 years). Initial body weight recordings for the men ranged between 48 and 85 kg, while the women at presentation weighed between 26 and 61 kg. A value for body weight was recorded at outpatient review between four and 12 months after commencement of the gluten-free diet in 45 of the patients. The men showed a mean weight gain of 7.2 kg and the women a gain of 6.6 kg.

Symptoms and clinical signs in all 50 patients at initial presentation are summarised in Tables I and II. Results of haematological and biochemical screening blood tests are illustrated in Tables III and IV. The spectrum of initial blood haemoglobin values and red cell mean corpuscular volume values in men and women are illustrated in the Figure.

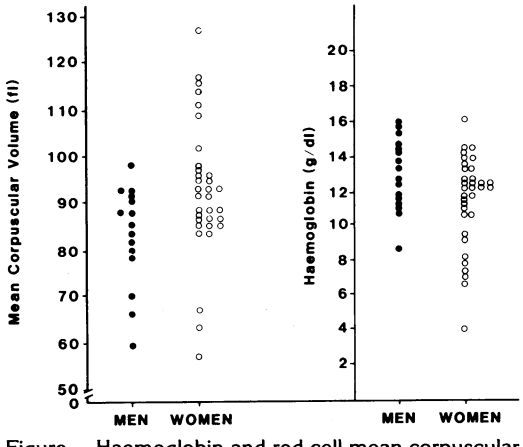


Figure. Haemoglobin and red cell mean corpuscular volume in men and women with coeliac disease.

TABLE I

*Presenting symptoms in 50 coeliac patients*

| *Symptom* | *% men (n = 16)* | *% women (n = 34)* | *% overall* |
|---|---|---|---|
| Weight loss | 56 | 47 | 50 |
| Diarrhoea | 75 | 74 | 74 |
| Steatorrhoea | 38 | 50 | 46 |
| Tiredness | 38 | 47 | 44 |
| Abdominal pain | 50 | 38 | 42 |
| Carpopedal spasm | 6 | 18 | 14 |
| Abdominal fullness | 12 | 9 | 10 |
| Vomiting | 0 | 12 | 8 |
| Constipation | 0 | 6 | 4 |
| Bone pain | 0 | 6 | 4 |

TABLE II

*Presenting signs in 50 coeliac patients*

| *Signs* | *% men (n = 16)* | *% women (n = 34)* | *% overall* |
|---|---|---|---|
| Skin pallor | 31 | 35 | 34 |
| Glossitis | 12 | 18 | 16 |
| Muscle wasting | 12 | 6 | 8 |
| Mouth ulcers | 12 | 18 | 16 |
| Peripheral oedema | 0 | 9 | 6 |
| Dermatitis herpetiformis | 6 | 3 | 4 |
| None | 63 | 32 | 42 |

TABLE III

*Haematology investigations at presentation*

| | *Abnormal value* | *% Abnormal men (n = 16)* | *% Abnormal women (n = 34)* | *% Abnormal overall (n = 50)* |
|---|---|---|---|---|
| Haemoglobin | <12 g/dl | 38 | 44 | 42 |
| Mean corpuscular volume | <84 fl | 38 | 9 | 18 |
| | >100 fl | 0 | 21 | 14 |
| Folic acid | <2.0 µg/l | 44 | 35 | 38 |
| Vitamin B12 | <200 ng/l | 13 | 21 | 18 |
| Iron — men | <16 µmol/l | 44 | — | 40 |
| women | <11 µmol/l | — | 38 | |
| Total iron binding capacity | >70 µmol/l | 31 | 32 | 32 |
| Prothrombin time | >15 seconds | 25 | 18 | 20 |
| ESR | >10 mm/1st hour | 25 | 47 | 40 |

TABLE IV

*Blood biochemistry tests at presentation*

| | *Number measured* | *Abnormal value* | *Number abnormal* | *% abnormal* |
|---|---|---|---|---|
| $Ca^{2+}$ | 50 | <2.20 mmol/l | 26 | 52 |
| $Mg^{2+}$ | 18 | <0.70 mmol/l | 3 | 17 |
| $Zn^{2+}$ | 12 | <8.4 µmol/l | 1 | 8 |
| Albumin | 48 | <30 g/l | 5 | 10 |
| | | <35 g/l | 13 | 27 |
| ALT | 9 | >45 i.u. | 3 | 33 |

Results of malabsorption tests are summarised in Table V. Only eight patients received a 25g dose of D-xylose and, of these, six had an abnormal result. Of the 33 patients who were given a 5g dose of D-xylose, 16 had an abnormally low urinary excretion.

TABLE V

*Malabsorption tests at presentation*

| | *Number measured* | *Abnormal value* | *Number abnormal* | *% abnormal* |
|---|---|---|---|---|
| Serum carotene | 30 | <1.1 µmol/l | 21 | 70 |
| Faecal fats | 8 | >5g/day | 6 | 75 |
| $C^{14}$ fat breath test | 29 | *Max value <20.0 | 24 | 83 |
| D-xylose test | 41 | <23% 5g<br><17% 25g | 22 | 54 |
| Glucose tolerance test | 31 | blood sugar rise<br><2.2 mmol/l | 26 | 84 |
| Urinary indican | 29 | >220 µmol/24 hour | 17 | 59 |
| Small bowel series | 37 | 'malabsorption picture' | 29 | 78 |

At the time of diagnosis of coeliac disease, two patients, one man and one woman, were found to have dermatitis herpetiformis. This condition developed subsequently in two other women eight and nine years after the detection of coeliac disease. Only one patient, a woman, developed a lymphoma, and this affected the larynx rather than the gastro-intestinal tract. The lymphoma was detected five years after the diagnosis of coeliac disease. One woman, who had unequivocal subtotal villous atrophy on jejunal biopsy, and who responded well to gluten withdrawal, developed hyperparathyroidism and then jejunal Crohn's disease eight years after coeliac disease had been diagnosed. Three patients had evidence of pancreatic exocrine insufficiency suggested by an abnormal PABA test (para-amino benzoic acid absorption). All three had persisting or recurrent gastro-intestinal symptoms.

A repeat jejunal biopsy after gluten withdrawal in adult patients with coeliac disease was not routine clinical practice during most of the period covered by our survey. Seventeen of our patients were re-biopsied recently, between one and 15 years after gluten was excluded from the diet. Thirteen patients were entirely asymptomatic, three had occasional abdominal cramps and diarrhoea, and one patient had a severe clinical relapse with weight loss and marked diarrhoea. The repeat jejunal biopsies were entirely normal only in six patients, and mild villous atrophy was seen in 10 patients. The patient with severe clinical relapse had subtotal villous atrophy and responded well to treatment with oral prednisolone. A careful dietary history taken at the time of repeat biopsy revealed that 44% of these patients continued, often unknowingly, to consume small amounts of gluten. The patient with clinical relapse appeared to be adhering strictly to a gluten-free diet.

## DISCUSSION

The wide spectrum of clinical findings in adult patients with untreated coeliac disease has been illustrated in this study. However, it is likely that our data underestimate the number of asymptomatic or mildly symptomatic individuals, since these people may not present themselves for investigation. If screening of families of coeliac patients became accepted clinical practice, it is possible that an even higher number of asymptomatic individuals would be identified.

Increasing awareness of the malabsorption disorders and increasing use of screening biochemical and haematological tests by hospital physicians and general practitioners might be expected to increase the detection of mild cases of coeliac disease. Only one of our patients was completely asymptomatic, although 22% had no disturbance of bowel habit. A higher incidence of diarrhoea was observed in some of the earlier studies (97% of patients in one report[2]) although the classic paper of Cooke and colleagues in 1953 described diarrhoea in only 80% of 100 patients with idiopathic steatorrhoea.[3]

Weight loss is regarded by many as a cardinal feature of the malabsorption syndrome and yet this symptom was only recorded in 50% of our patients. Minor degrees of weight loss may not have been noted by some individuals. Many adult patients are likely to have been malabsorbing to some extent for long periods of time before the hospital assessment, and a failure to maintain adequate weight rather than weight loss may have been a feature of their illness. Earlier retrospective surveys of symptoms in coeliac patients recorded weight loss as a feature in 97-100% of patients.[2, 3]

An important symptom in many of our patients was abdominal pain or fullness. An erroneous diagnosis of irritable bowel syndrome may be suggested by these findings unless malabsorption is given due consideration. The more specific symptom of tetany was observed in only 14% of patients in contrast to 38-50% of patients in earlier studies.[2, 3]

Abnormal findings on physical examination were detected infrequently in our survey. It is surprising that no patient was recorded to have finger clubbing or abnormal pigmentation as these signs have been well documented in severe coeliac disease.[3] Earlier presentation to hospital for diagnosis in recent years may have influenced the development of signs normally associated with severe long-standing disease, but it is also possible that subtle alterations in skin pigmentation or mild clubbing were overlooked or not recorded by the admitting physicians.

Screening blood tests frequently raise the suspicion of malabsorption. A low blood haemoglobin level was found in only 42% of our patients, which illustrates the danger in relying on such tests to exclude the presence of malabsorption. Cooke and Holmes[4] also detected a haemoglobin level of <12 g/dl in 42% of 170 coeliac patients in England, although an Australian survey described anaemia in 70% of patients.[5] A macrocytic blood picture was detected in only 14% of our study group. Folate deficiency is the commonest cause and a serum folate level of <2.0 µg/l was found in 38% of patients. The absence of macrocytosis in some of these individuals was probably related to coexistent iron deficiency. Hallert and colleagues[6] noted low serum folate levels in 85% of coeliac patients and found a high yield of coeliac disease when patients with unexplained low folate levels were subjected to jejunal biopsy. Vitamin $B_{12}$ deficiency is a less frequent abnormality as this is normally absorbed in the terminal ileum which usually remains free of mucosal damage. Of our patients 18% had a low serum $B_{12}$ level, but in some of these individuals fast small bowel transit rather than terminal ileal damage may have produced impaired absorption of this vitamin. Only 18% of our patients had a microcytic blood picture but this finding was more common in males. The explanation for the difference between males and females is not clear. Iron deficiency was suggested by a low serum iron in over 40%, and by a high total iron binding capacity in 32% of the group. Associated folate or $B_{12}$ deficiency may have prevented the development of microcytosis in some of these individuals.

With regard to the blood biochemistry tests, hypoalbuminaemia reflects impaired protein synthesis and, in some cases, protein loss into the gastro-intestinal tract. Early reports described this finding in over 50% of patients with coeliac disease,[2,7] although a recent survey had detected serum albumin levels of <40 g/l in 28% and <30 g/l in only 4% of patients.[4] Our findings are fairly similar, 27% of patients having a serum albumin <35 g/l and 10% a level <30 g/l. Hypocalcaemia might simply reflect the low serum albumin concentration, but 52% of our patients had low serum calcium levels — a higher percentage than had hypoalbuminaemia. When the serum calcium level was corrected for the serum albumin level only 3 of the abnormal results became normal, so it is likely that most hypocalcaemia was due to true calcium or vitamin D deficiency as part of the malabsorption syndrome.

Several investigations aid definition of the type of malabsorptive disorder and some of these have been regarded as valuable screening tests for coeliac disease. The D-xylose test assesses passive absorption of a non-digestible sugar across the small bowel mucosa. Abnormal results were recorded in over 90% of patients in two surveys,[8,9] but other investigators have questioned its value.[10,11] In our survey, only 54% of patients had an abnormal D-xylose excretion. Most received a 5g load of xylose, but of those eight patients who were given 25g xylose, 75% had abnormal results. Rinaldo and Gluckman (1964) also found that a 5g load of D-xylose was less efficient than the 25g dose at detecting coeliac disease.[12] Clearly, reliance on the D-xylose test as a screening test to exclude malabsorption syndrome is misplaced and normal results with this investigation should not deter a clinician from proceeding to jejunal biopsy. Although 84% of patients had a flat glucose tolerance test, the value of this investigation is hindered by the occurrence of a flat response in a significant proportion of the normal population.[13]

Steatorrhoea is a classical feature of coeliac disease and several investigations give useful information regarding fat absorption. The traditional three-day collection of faeces for fat content was carried out in only eight patients and 75% of these had abnormal results. Fat breath tests measure the radioactivity of expired air after ingestion of a triglyceride labelled with $^{14}C$. Tripalmitate has been used in the Royal Victoria Hospital with satisfactory results for some years,[14] although American investigators found that the $^{14}C$ triolein breath test provided more reliable discrimination, mainly due to greater specificity.[15] Of 29 patients in our study who had a tripalmitate breath test 83% had an abnormal result, which is not sufficiently sensitive to allow accurate selection of patients for jejunal biopsy.

Our observations have highlighted the clinical features of coeliac patients in adult gastroenterological practice in Northern Ireland. It appears that milder forms of the disease are being recognised than was the case in the 1950s when the condition was first defined. The presence of severe villous atrophy is rarely seen in conditions other than coeliac disease in adult patients, although this is not the case with children. In clinical practice a more difficult group to classify are those adult patients whose jejunal biopsies show only mild or moderate villous atrophy, findings which can be caused by many disorders. Some of these individuals were encountered in our survey, and although they had been treated by gluten withdrawal, they were not included in this analysis. Similarly, there were two or three individuals who were treated by gluten withdrawal, but for whom no histological confirmation of the diagnosis of coeliac disease was made because of technical failure of the Crosby capsule biopsy instrument. A repeat jejunal biopsy after gluten withdrawal followed by a period of gluten challenge and further biopsy would be of particular value in the assessment of these groups of patients whose diagnosis is less well established, before lifelong gluten avoidance is imposed.

A wide spectrum of haematological and biochemical disturbances may occur in coeliac patients but no single test offers a reliable method of screening for the condition. Tests of absorptive function have failed to identify sufficient patients to serve as reliable screening tests for coeliac disease. Better screening tests are required so that milder forms of the condition may be identified. Serum anti-gliadin antibody determination[16] and release of N-terminal glucagon[17] have been proposed as possible screening tests but further assessment of their sensitivity in adult patients is required. The former reflects the immunological response to gliadin, which is thought to be the toxic component of gluten, and abnormal levels have been found in about 90% of coeliac patients.[16] Release of N-terminal glucagon probably reflects increased stimulation of the distal ileum by food which is malabsorbed in the jejunum.[17] Thus, elevated plasma levels of this hormone are not specific to coeliac disease and are encountered in a variety of conditions associated with small bowel malabsorption. Jejunal biopsy with a Crosby capsule remains the definitive investigation to identify patients with coeliac disease. This procedure can be performed rapidly and without significant discomfort during upper endoscopic examination,[18] and should be undertaken when the diagnosis of coeliac disease is considered.

We are indebted to our predecessors in the Gastroenterology Unit, Royal Victoria Hospital, whose careful documentation of their coeliac patients made our survey possible.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 148 – 154, October 1985.

# A histomorphometric study of osteomalacia in elderly females with fracture of the proximal femur

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Accepted 30th August 1985.


## SUMMARY

*Using standard histomorphometric indices on bone biopsies of trabecular bone volume, osteoid volume, the trabecular osteoid surface, the extent of the calcification front and the number of osteoid lamellae, a histomorphometric diagnosis of osteomalacia was made in three of 28 elderly female patients with fracture of the proximal femur. These patients also showed biochemical changes in the serum and deficiency of serum vitamin D. The 25 biopsies judged not to show osteomalacia showed a greater osteoid volume in the 12 patients who suffered an intertrochanteric fracture than in the 13 with a cervical fracture. Clinical biochemistry in these 25 patients showed considerable overlap between the normal range and that found in the patients with osteomalacic biopsies.*


## INTRODUCTION

Proximal femoral fracture is predominantly a problem of the elderly, affecting females over twice as commonly as males, and with an exponential rise in incidence with increasing age. This common problem in elderly females has been attributed in part to a reduced bone mass as a consequence of postmenopausal osteoporosis. Osteoporosis is defined as a condition in which the absolute amount of bone is diminished while the remaining bone is normal, whereas osteomalacia is characterised by deficient mineralisation of normal bone matrix.

The importance of osteomalacia as a preventable cause of fracture of the proximal femur has attracted considerable attention, particularly as treatment with vitamin D reverses the defective mineralisation of bone. However, the role of osteomalacia as a contributory factor to the aetiology of proximal femoral fracture remains in dispute. Histological evidence of osteomalacia has been reported in 20% of proximal femoral fracture patients from Scotland,[1] 30% from Wales,[2] 16-34% of females from Leeds[3] and 33% of females from London.[4] Other series of patients in Scotland and England have shown histological evidence in only 10% or less of fracture patients.[5-7] A large part of the variation between these studies can be attributed to the different histological criteria used to diagnose osteomalacia. In addition to differing methods of measurement, different parameters were employed which included osteoid volume,[1, 2] osteoid surface and mineralisation front,[3] and osteoid thickness.[5, 6] Nevertheless, there

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appears to be an increased prevalence of osteomalacia among elderly patients with proximal femoral fracture, which may predispose to the fracture. Such fractures appear likely to result either from the reduced strength of osteomalacic bone or from the myopathy associated with osteomalacia resulting in reduced mobility and an increased risk of falls.

## PATIENTS

Between August 1983 and July 1984, bone biopsies were obtained at the time of surgery for internal fixation of proximal femoral fracture from 28 female patients over age 65 years. The indications for biopsy were either as part of a research study approved by the ethical committee of treatment regimes for osteoporosis, or because osteomalacia was suspected on clinical or biochemical grounds. The former group (24 patients) were mentally alert and receiving few drugs and were considered unlikely to have osteomalacia, while the latter group (four patients) were considered likely to have osteomalacia.

## METHODS

Iliac crest biopsies were obtained in 26 subjects using a transiliac biopsy trephine, and in two subjects samples were obtained from the excised femoral head. The biopsies were prepared undecalcified, embedded in methyl methacrylate following the method of Difford[8] and sectioned using a motorised microtome. Sections were stained with aqueous toluidine blue which stains mineralised bone purple and osteoid blue, and also with an ethylene diamine tetra-acetic acid solution of toluidine blue which stains mineralised bone pink, osteoid light blue and the calcification front dark blue (Fig 1). The undecalcified sections obtained from the centre of the specimens were quantified using a planimetry system (MOP Videoplan Image Analysis System). The movable image of a liquid crystal diode was superimposed on the imaged field of the stained sections, enabling measurement to be carried out of the area of trabecular bone, area of osteoid, total length of trabecular surfaces and length covered by osteoid, and the proportion of osteoid surfaces with a calcification front. The maximum numbers of birefringent lamellae of osteoid were observed and counted at 100 × magnification under polarised light (Fig 2). The following histomorphometric indices were calculated from the measurements:

$$\text{Trabecular bone volume (TBV) \%} = \frac{\text{Area of trabecular bone (osteoid + mineralised)}}{\text{Total area (trabecular bone + inter-trabecular area)}} \times 100$$

$$\text{Relative osteoid volume (ROV) \%} = \frac{\text{Area of osteoid}}{\text{Area of trabecular bone (osteoid + mineralised)}} \times 100$$

$$\text{Relative trabecular osteoid surface (ROS) \%} = \frac{\text{Trabecular surface length covered by osteoid}}{\text{Total surface length of trabecular bone}} \times 100$$

$$\text{Extent of calcification front (CF) \%} = \frac{\text{Surface length of osteoid with calcification front}}{\text{Surface length of osteoid}} \times 100$$

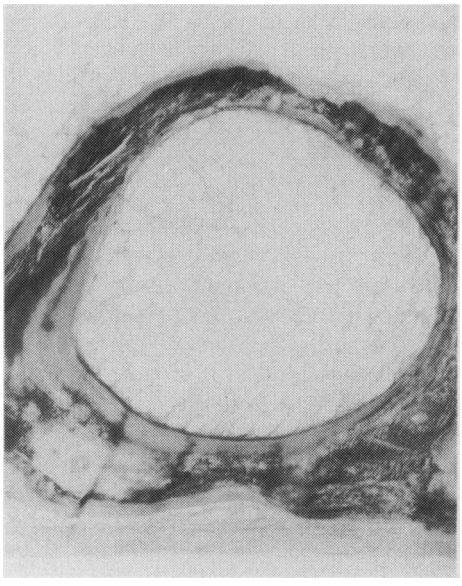
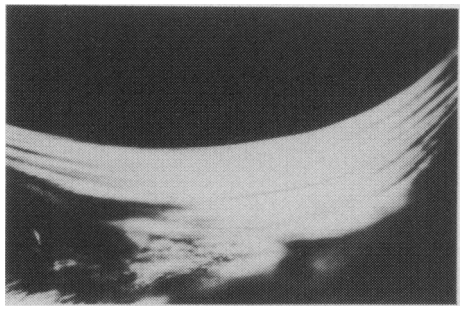


Fig 1 (left). Undecalcified section of iliac crest biopsy with trabecular surfaces covered by a thickened layer of osteoid indicative of osteomalacia (Case 1). Toluidine blue stain, × 100.

Fig 2 (below). Osteoid seam with lamellar pattern viewed under polarised light (Case 3), × 200.



A histological diagnosis of osteomalacia was considered if the relative osteoid volume was $>3.5\%$, the relative trabecular osteoid surface $>24\%$, the calcification front $<60\%$, or the maximum number of birefringent osteoid lamellae in excess of three.

A venous blood sample was withdrawn at the time of admission to estimate corrected serum calcium,[9] serum phosphate, alkaline phosphatase, albumin, globulin, urea, 25-hydroxyvitamin D (25 OHD) and 1,25 dihydroxyvitamin D (1,25 $OH_2D$) levels. Fractures were divided into cervical and intertrochanteric (including basal cervical), according to radiographic appearances. Results were analysed using the Mann-Whitney U test, and mean and standard deviation calculated for comparisons between groups.

## RESULTS

Sixty-four female patients with proximal femoral fracture were admitted during the study period, and satisfactory histological analyses of undecalcified bone biopsies obtained in 28 of these. Their histomorphometric indices are shown in Table I and biochemical measurements in Table II. Three of these patients (11%) had histomorphometric evidence of osteomalacia. These three patients had already been suspected on the basis of a raised serum alkaline phosphatase in all three, low serum phosphate in two, and a low serum calcium in one. The two patients who had not received supplementary vitamin D had very low serum 25-hydroxyvitamin D and plasma 1,25 dihydroxyvitamin D. The mean values of these biochemical measurements in the two fracture subgroups judged not to have osteomalacia showed no significant differences. The corrected serum calcium was low in four of these patients, serum phosphate was low in one, serum alkaline phosphatase elevated in nine, and serum 25-hydroxyvitamin D was less than 25 nmol/l in 14 patients.

TABLE I

*Histomorphometric indices in three patients judged to have osteomalacia, and in 25 patients judged not to have osteomalacia. The patients without osteomalacia have been divided into a group of 13 with cervical fracture and a group of 12 with intertrochanteric fracture*

| | *Trabecular bone volume (%)* | *Relative osteoid volume (%)* | *Relative trabecular osteoid surface (%)* | *Calcification front (%)* | *Maximum number osteoid lamellae* |
|---|---|---|---|---|---|
| OSTEOMALACIA | | | | | |
| Case 1 | 22 | 9.0 | 72 | 78 | 5 |
| 2 | 26 | 11.6 | 89 | 58 | 3 |
| 3 | 19 | 12.3 | 23 | 48 | 4 |
| NO OSTEOMALACIA | | | | | |
| Cervical fracture | 19.6 | 0.92* | 7.8 | 83.5 | 1.5 |
| (n = 13) (mean ± SD) | (± 6.6) | (± 0.6) | (± 7.6) | (± 4.6) | (± 0.7) |
| Intertrochanteric fracture | 15.9 | 2.02* | 10.7 | 79.3 | 1.4 |
| (n = 12) (mean ± SD) | (± 6.6) | (± 1.1) | (± 6.8) | (± 9.1) | (± 0.5) |

*Significant difference p = 0.01.

TABLE II

*Biochemical measurements in the three patients judged to have osteomalacia and in the two groups of patients judged not to have osteomalacia*

| | *Corrected serum calcium (mmol/l)* | *Serum phosphate (mmol/l)* | *Serum alkaline phosphatase (IU/l)* | *Serum urea (mmol/l)* | *Serum 25-OH D (nmol/l)* | *Plasma 1,25 $OH_2D$ (pmol/l)* |
|---|---|---|---|---|---|---|
| OSTEOMALACIA | | | | | | |
| Case 1 | 2.22 | 0.88 | 423 | 12.3 | 9 | <11 |
| 2 | 2.21 | 0.63 | 243 | 10.3 | 71* | 49* |
| 3 | 2.11 | 0.54 | 394 | 9.7 | 4.5 | <10 |
| NO OSTEOMALACIA | | | | | | |
| Cervical fracture (n = 13) (mean ± SD) | 2.28 (± 0.1) | 1.03 (± 0.2) | 175.1 (± 50) | 8.8 (± 3.7) | 23.7 (± 18) | 17.4 (± 11.1) |
| Intertrochanteric fracture (n = 12) (mean ± SD) | 2.30 (± 0.1) | 1.02 (± 0.1) | 179.2 (± 36) | 8.2 (± 3.1) | 26.1 (± 12) | 18.2 (± 7.6) |

*Vitamin D therapy had been commenced three weeks before the proximal femoral fracture.

The relationship between corrected serum calcium and serum 25-hydroxyvitamin D is shown in Fig 3. Neither of these measurements identified all three of the osteomalacic patients. A considerable number of the patients not judged to be osteomalacic have low values of one or the other, or both, measurements.

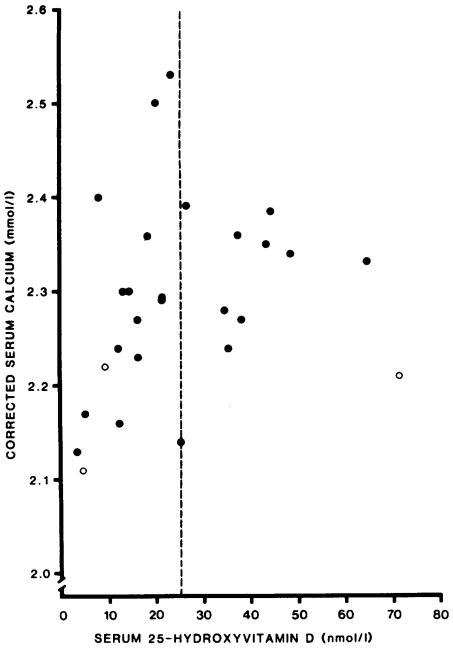



Fig 3. Serum calcium and 25-hydroxyvitamin D (normal > 25 nmol/l) in elderly females with proximal femoral fracture with (o) and without (●) histomorphometric evidence of osteomalacia.

The biopsies in 25 patients showed no histomorphometric evidence of osteomalacia. One patient with radiological evidence of Paget's disease of bone involving the pelvis had accompanying histological evidence with increased woven bone within the trabeculae compatible with this diagnosis. These 25 patients have been subdivided into 13 with a cervical fracture (mean age 80 years) and 12 with an intertrochanteric fracture (mean age 81 years). The only significant difference between these two groups was that the relative osteoid volume was greater for those with an intertrochanteric fracture, although none reached the level necessary for classification of osteomalacia.

## DISCUSSION

Osteomalacia was confirmed in three of 28 (11%) elderly female patients with proximal femoral fractures selected for this study. Selection was conducted neither randomly nor in a controlled prospective fashion and these patients may therefore not fully represent the population from which they were drawn. Those with low mental test scores, who are more frail and have an increased likelihood of vitamin D deficiency, were excluded from the research study group (24 patients), while the other four patients were considered likely to have osteomalacia. The prevalence of osteomalacia was similar to the 10% reported in a study of patients with proximal femoral fracture in Glasgow,[7] in which similar histological diagnostic criteria were used, and where latitude and hours of sunlight are comparable with those in Belfast.

The biochemical results emphasise that corrected serum calcium measurements may be normal in patients with osteomalacia.[10] Similarly, serum phosphate may be unhelpful[11] although hypophosphataemia often precedes the development of hypocalcaemia.[12] The serum alkaline phosphatase was markedly elevated in the patients with osteomalacia, and, although this abnormality is not specific, the elevation as a consequence of fracture alone was usually less than twice the upper limit of normal (340 IU/l) and indeed was not elevated in 16 cases (57%) at the time of admission. The two patients with untreated osteomalacia had serum 25-hydroxyvitamin D levels of less than 25 nmol/l (10 ng/ml), the level below which osteomalacia is considered to occur.[13] However, 14 patients had markedly lowered serum 25-hydroxyvitamin D values but without histomorphometric changes of osteomalacia, which confirms that low values in the elderly may occur in the absence of osteomalacia.[14]

Increased trabecular bone volume[15, 16] and reduced amount of osteoid[17] in patients with cervical fractures in comparison with trochanteric fractures have

been noted previously. In this series there was no significant difference in mean serum 25-hydroxyvitamin D levels between the two fracture groups, although lower 25-hydroxyvitamin D values[13] and a higher incidence of osteomalacia have been reported in trochanteric fractures.[18] While the increased amount of osteoid in patients with trochanteric fractures may occur as a consequence of deficiency of vitamin D and a mild mineralisation defect, the poorer physical status and accompanying disease processes in this type of fracture may be of equal importance, causing increased bone turnover and a resultant overall increase in bone resorption.

The incidence of osteomalacia amongst elderly hospital admissions has been shown to be highest in females and those over 70 years of age.[19] This same population also carries the highest risk of sustaining a fracture of the proximal femur, and thus the two conditions may occur together without the relationship being causal. Minor increases in osteoid have been associated with an increased risk of fractures of the proximal femur,[3, 17, 20] and bone strength has been shown to be significantly related to the amount of osteoid.[1] Careful screening of fracture patients to identify this preventable factor must be important, since even at this late stage treatment with calciferol, which is simple, cheap and effective, will aid fracture healing[11] and prevent further fractures. Additionally, the resolution of musculoskeletal symptoms accompanying osteomalacia is of considerable symptomatic benefit to the patient with consequent improvement of mobility and independence.

I wish to thank Mr JW Calderwood, Mr NW McLeod, Mr JR Nixon and Mr JB Pyper for permission to study patients under their care, and Mr BF Craig, Mr AH McMurray, Mr PC Pyper and Mr AR Wray for providing peroperative bone biopsies. I also gratefully acknowledge the help of Mr J Orchin and Mr D Harvey in the preparation of biopsy sections, Dr JD Biggart for histological advice and facilities, Dr PCH Watt and the Department of Pathology, Royal Victoria Hospital, for use of the MOP-Videoplan System, and Dr RA Cowan and Armour Pharmaceutical Co Ltd for measurement of 1,25 $(OH)_2D$ levels. During much of this work I was in receipt of a Research Fellowship from the Department of Health and Social Services (Northern Ireland).

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 155 – 159, October 1985.*

# Peritoneovenous shunting in intractable ascites

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Accepted 25th July 1985.


## SUMMARY

*Fourteen patients in whom peritoneovenous shunts were inserted for intractable ascites or malignancy were reviewed.*

*Reduction in ascites was obtained in all patients by the time of discharge with significant diuresis and weight loss. Significant decrease in haemoglobin, packed cell volume, platelet count and prothrombin time also occurred. Coagulation studies were abnormal in 60 per cent of patients in whom they were performed with bruising or detectable bleeding occurring in 28.5 per cent of all patients. Late blockage of the shunt occurred in five patients and was less frequent in Denver than in Le Veen type shunts.*

*Cumulative mortality one month after shunt insertion was 28.5 per cent and at one year was 78.5 per cent reflecting the severity of the underlying disease.*

*Peritoneovenous shunting should be reserved for palliation in patients resistant to full conventional medical therapy.*


## INTRODUCTION

In peritoneovenous shunting, ascitic fluid is returned to the venous circulation using a device consisting of silicone tubing and a one-way valve. A short general anaesthetic is required to insert one end of the shunt into the peritoneal cavity, tunnel the shunt subcutaneously over the rib cage and insert the venous end into the internal jugular vein. Peritoneovenous shunting is successful in the management of resistant ascites in cases of portal hypertension or malignancy. Several complications of the technique have, however, been reported.[1]

We present the limited experience of one unit with peritoneovenous shunting in patients with medically resistant ascites. Medical therapy included bed rest, salt restriction, water restriction and Frusemide and Spironolactone in doses up to 120 mg and 400 mg respectively daily.

## PATIENTS

Fourteen consecutive patients in whom peritoneovenous shunts were inserted were reviewed. There were 12 males and two females. The mean age was 55.2 years (range 23-78 years). Ascites was secondary to alcoholic cirrhosis in seven

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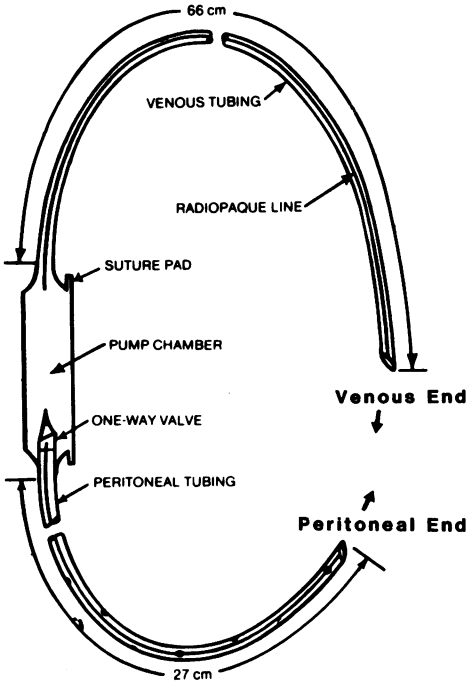


Fig 1. Diagram of Denver type of peritoneo-venous shunt (With permission of Downs Surgical Limited).

patients, to cryptogenic cirrhosis in four, to malignancy in two (one primary hepatocellular carcinoma and one adenocarcinoma of the stomach) and a further patient had severe Budd-Chiari syndrome. Two of the patients with alcoholic cirrhosis were subsequently shown to have hepatocellular carcinoma after insertion of the shunt. In the cirrhotic group there were seven patients in Child's grade C category and five in Child's grade B.

Six LeVeen and eight Denver shunts were inserted (Fig 1). Less than half a litre of ascitic fluid was removed at the time of inserting the shunt. Reduction of ascites was assessed using girth measurements, weight loss and urine output. In eight patients Frusemide was used to promote diuresis postoperatively. In some patients the rate of flow through the shunt was increased by using the technique of intermittent sucking through a straw to increase the negative intrathoracic pressure. Values of sodium, potassium, urea, creatinine, bilirubin, alanine transaminase, total protein, albumin, haemoglobin, packed cell volume, platelet count and prothrombin time before and after shunting were compared using the Wilcoxan Signed Rank Test for non-parametric paired data.

## RESULTS

All but one patient had lost weight by the end of the first postoperative week; the mean weight loss was 4.6 kilograms ($p < 0.01$). Figure 2 shows the increased mean urinary output on the third postoperative day ($p < 0.01$) but by the end of the first week this had tailed off. The haemoglobin values fell from 13.6 to 11.2 gm/dl ($p < 0.05$), and packed cell volume from 0.396 to 0.339 ($p < 0.01$). The platelet count fell postoperatively from 187 x $10^3$/L to 102 x $10^3$/L ($p < 0.05$). Prothrombin time decreased in all 10 patients in whom it was measured (mean values 54 to 30 per cent ($p < 0.01$). No statistically significant changes occurred in the other blood tests.

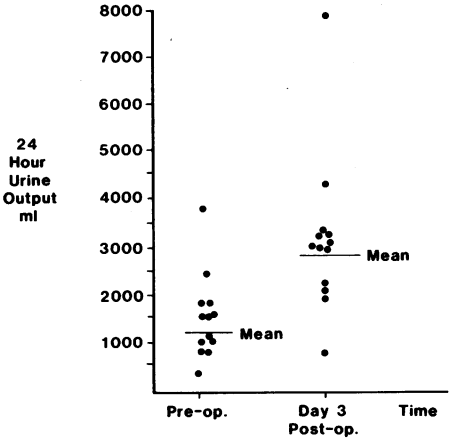


Fig 2. The 24-hour urine output preoperatively and on the third postoperative day. The changes were significant using the Wilcoxan Signed Rank Test ($p < 0.01$).

## MORBIDITY

Abnormalities of coagulation were common after shunt insertion. Full coagulation studies were performed in 10 of the 14 patients and were abnormal in six. Clinically detectable bleeding from the wound, gastrointestinal or genitourinary systems was noted in four patients. Excessive bruising occurred in a further two cases and one patient died on the third postoperative day from uncontrollable disseminated intravascular coagulation.

Two patients developed ascitic leaks postoperatively and one of these subsequently developed staphylococcal septicaemia. Although this was initially controlled by antibiotics, one month later further septicaemia and staphylococcal ascitic infection proved fatal. One other patient died of staphylococcal septicaemia 20 days after insertion of the shunt. Two patients developed pulmonary oedema to some degree on the first and second postoperative days respectively, and both responded to conventional medical therapy. One patient bled from oesophageal varices on the second postoperative day but this settled with conservative management. Late blockage of the shunt occurred in five patients after an average of 10 months (range one to 30 months). Of the six episodes of blockage, four occurred at the abdominal catheter and only two at the venous catheter.

## MORTALITY

Three patients died during the hospital admission in which the shunt was inserted. One died on the third postoperative day from disseminated intravascular coagulation, the other two from liver failure on the thirteenth and fourteenth postoperative days respectively. Of the 11 patients who survived to leave hospital, nine subsequently died after a mean survival of nine months (range three weeks to 40 months). Death was due to liver failure in four patients and, in two of these, hepatocellular carcinoma was documented prior to death. Other causes of mortality were infected ascites in two, carcinoma in two and variceal haemorrhage in one. The cumulative mortality was 28.5 per cent one month after operation; 42.8 per cent at two months; 57 per cent at six months and 78.6 per cent at one year. Only two patients still survive, one five years, the other seven years after insertion of their shunts.

## DISCUSSION

The vast majority of patients with ascites of cirrhotic origin can be successfully managed with low sodium intake, fluid restriction and diuretics. Diuretics, however, contract the extracellular fluid compartment and this may induce renal failure refractory to further therapy. Failure to respond to medical management has been reported in 4.5 per cent of ascitic patients.[2] Intermittent intravenous reinfusion of ascitic fluid was seen to bring transient relief of ascites. In attempts to produce sustained relief a variety of the neurosurgical pressure activated shunts were tried.[3,4] In 1974 LeVeen introduced a peritoneovenous shunt specifically designed for management of resistant ascites.[5] The Denver shunt modification allows manual pumping of the valve.[6] These devices allow the peritoneal cavity to be drained through a one-way valve into a central vein. During inspiration the intraperitoneal pressure rises while the intrathoracic pressure falls; pressure differences of greater than four centimetres of water can then propel ascitic fluid into the central vein.

Peritoneovenous shunting is effective in reducing ascites. The weight loss and increased urine output in our patients cannot be attributed to the fluid volume removed on inserting the shunt, or to paracentesis alone. Indeed the degree of

weight loss and diuresis in our patients was similar to that reported in other series.[7, 8, 11] A fall in packed cell volume has been used as a measure of the effective transfer of fluid into the venous circulation.[8, 9] Although a statistically significant fall in packed cell volume occurred in our series, it was accompanied by a concomitant fall in haemoglobin which may, in part, account for the change. Bernhoft reported 84 per cent control of ascites at two months, 65 per cent at six months and 50 per cent at one and two years, which is slightly better than our findings.[9] In the hepato-renal syndrome, however, the results appear more variable. There are several reports of improvement[1, 7, 10, 11] although, in some of these, strict criteria for the syndrome may not have been applied.[12] The absence of statistically significant changes in total protein and albumin in our series is surprising, for it is assumed that the transfer of protein into the vascular compartment contributes to the reduction in ascites. Greenlee obtained similar results but noted that significant changes in protein concentration occurred six months after shunting.[2]

Coagulation abnormalities after shunt insertion are well recognised, the reported incidence varying from 20 to 91 per cent.[7-16] The incidence of coagulation abnormalities and detectable bleeding in our series is comparable with the observations of most authors.[7, 11, 13, 15] The triggering factor in the fluid has been ascribed to endotoxin, thromboplastin and activated clotting factors. Schwartz[14] and Ragni[15] believe that coagulopathy is related to release into the systemic circulation of ascitic fluid rich in fibrin degradation products. Treatment of the coagulopathy has consisted of heparin, epsilon-amino-caproic acid and infusion of blood products.[7] Infusion of antithrombin III appears ineffective.[16] Removal of an amount of ascitic fluid at the time of operation may reduce the risk of disseminated intravascular coagulation but results appear variable.[1, 8, 13] Spontaneous resolution of the abnormal coagulation tends to occur towards the end of the first postoperative week,[14] but, in severe cases, ligation of the shunt has been advocated to stop progression of the coagulopathy.[7]

Bleeding from oesophageal varices after shunting is related to expansion of the blood volume with resultant increase in portal pressure, and removal of a large amount of ascitic fluid at operation may reduce this possibility. LeVeen suggests that shunting should be performed only after decompression of the portal system.[7] Leakage of ascitic fluid is a commonly recognised problem after shunting.[7-9, 12] If the ascitic fluid becomes infected, mortality is high. Greenlee found infection a major factor in his early postoperative deaths, stating that preoperative ascitic fluid cell counts and culture should be performed to lessen the risk of shunting infected ascites. Foreign bodies such as catheters or intravenous cannulas should be removed early to minimise sources of potential infection. The low incidence of blocked Denver shunts compared with LeVeen in our survey confirms previous reports;[17, 19] it is related to the percutaneous pumping chamber of the Denver shunt which allows dislodgement of fibrin clots.

Significant symptomatic relief of ascites was obtained in our patients, tallying with the findings of other authors.[19-22] A major concern of shunting in malignant disease is the systemic dissemination of tumour cells, but this is usually not important in the short-term survival expected. Maat reported such a case[23] and Berger has noted subcutaneous tumour growth along the shunt.[24] Unfortunately blockage of the shunt is not uncommon in patients with malignant ascites.[22] The high cumulative mortality reflects the severity of the underlying disease process in the patients who were considered for shunting. In liver disease, Child's grading

correlates with survival after shunting, the poorest prognosis occurring in those patients with functional renal failure.[25, 26, 27]

Our study confirms that peritoneovenous shunting is effective in treating intractable ascites. However, morbidity and mortality are such that the technique should be reserved for cases resistant to full dose medical therapy.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 160 – 164, October 1985.*

# An audit of asthma in a Belfast practice

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Accepted 15th August 1985.

## SUMMARY

*One hundred and twenty-two asthmatic patients were identified with the help of a microcomputer in a Belfast practice of 3140. Thirteen different diagnostic labels were found to be used with up to five different labels used for a single patient. Inadequate treatment was found in a small number of patients, which was attributable to both doctor and patient. Regular monitoring using peak expiratory flow occurred in just 14 per cent. More frequent use of peak expiratory flow monitoring both in the surgery and at home and better patient education may go some way to reducing asthma morbidity and mortality.*

## INTRODUCTION

Deaths from asthma have failed to decline since the epidemic of the mid-1960s, with 1500 patients dying per year in England and Wales.[1] The British Thoracic Association in their study in 1982[2] found that avoidable factors were involved in 82 per cent of deaths. Delay in starting appropriate treatment was the single most important factor, due mainly to the failure of patients to recognise the severity of the attack. Poor patient education and control, and the infrequent use of steroids were also found to be significant. This study suggested to the authors the need to perform an audit of asthma in an urban practice of 3140 patients, with objectives which might point the way to improved patient management and education in the future.

## METHOD

Patients who had at some time been given a diagnostic label of asthma, or who had taken one or more drugs commonly used for asthma, were identified through the practice microcomputer.

Their A4 records were then assessed for appropriate history, investigations, drug therapy, monitoring of progress, the degree of severity and hospital admissions. Further information was obtained using a postal questionnaire completed independently by each patient. Defaulters were followed up. Analysis was carried out using a mainframe computer.

## RESULTS

One hundred and twenty-two patients were identified. There were 63 males and 59 females (48.4%), ranging from 1-81 years, with a mean age of 35 years. The prevalence of patients labelled asthmatic in the practice was 3.9 per cent.

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Thirteen different diagnostic labels were used to describe asthma in these patients, of whom 67 (54.9%) had just one label, 41 (33.6%) had two, 10 (8.2%) had three, two (1.6%) had four, and two (1.6%) patients had five labels. The commonest label was asthma in 89 (73.0% of patients), followed by wheezy bronchitis in 30 (24.6%), bronchial asthma in 17 (14.0%), asthmatic bronchitis in 12 (9.8%), wheezy tendency in nine (5.4%), and late onset asthma in seven (5.7%). Ninety-one patients (74.6%) had mild asthma, 22 (18.0%) had moderate asthma and nine (7.4%) had severe asthma. (See Table I for definitions).

TABLE I

*Definition of severity groups in asthma*

| | |
|---|---|
| Mild asthma | Intermittent airways obstruction which responds completely to inhaled or oral bronchodilators. |
| Moderate asthma | Low grade recurrent or continuous airways obstruction, requiring intermittent or continuous bronchodilator therapy +/or inhaled steroids.<br>May require oral steroids occasionally. |
| Severe asthma | Recurrent or continuous marked airways obstruction requiring recurrent or continuous bronchodilator therapy and inhaled steroids, complemented by short or long-term oral steroids. |

Seventy patients (57.4%) were considered to be atopic. Forty-eight (39.3%) indicated on the questionnaire that their attacks were precipitated by specific allergens of which house dust was the most common, followed by pollens, animal dander and house dust mite. Twenty-two patients (18.0%) had had skin testing and 21 (17.3%) had had immunotherapy. Other precipitating factors were found as indicated in Table II.

TABLE II

*Other precipitating factors for asthma*

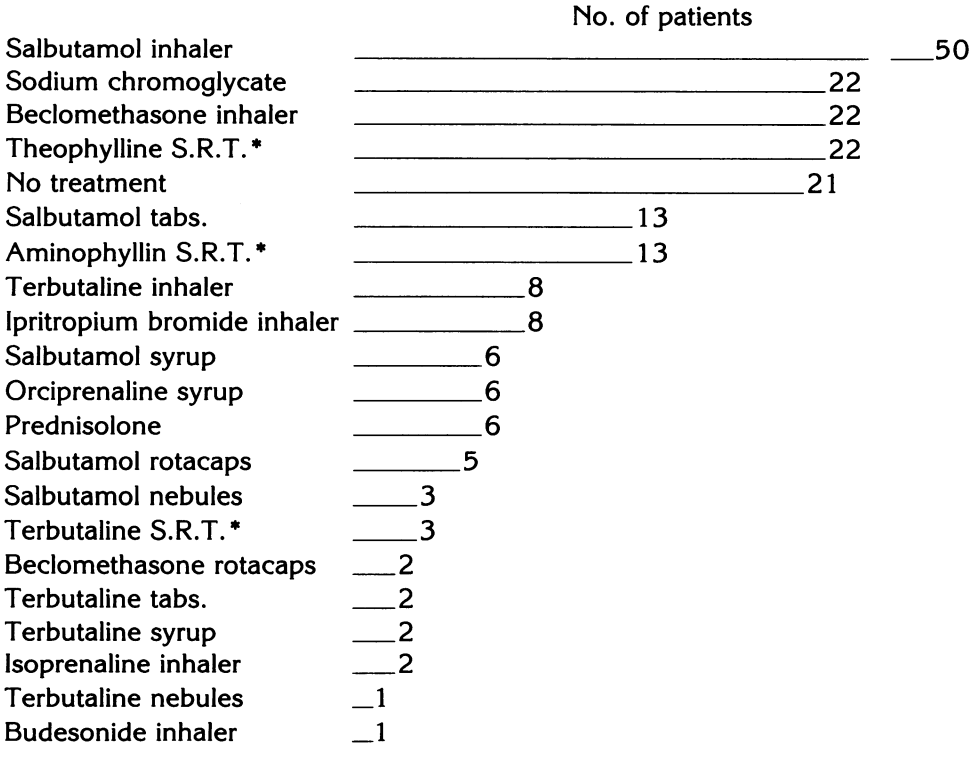
| | | |
|---|---|---|
| DIURNAL VARIATION 94 (77%) | Symptoms maximum at night | 80 (65.6%) |
| | Symptoms maximum by day | 14 (11.4%) |
| EMOTIONALLY INDUCED ATTACKS | | 43 (35.2%) |
| EXERCISE INDUCED ATTACKS | | 31 (25.4%) |
| EXERCISE + EMOTIONALLY INDUCED ATTACKS | | 31 (25.4%) |

A history of smoking was recorded in only 26.9% of the adults. Nineteen patients (15.6%) smoked and 20 of the 33 children lived with smokers. Twenty-one patients (17.2%) were not taking any drugs. Of these patients, four considered themselves to have had no troublesome attacks in the last year, nine had had one, three had had two, three had had three, and two had had six attacks. One of these last two patients, a 14-year-old, complained of continuous wheeze and cough and yet had attended the general practitioner only once. The other patient, a four-year-old, had had frequent episodic symptoms and had attended the

general practitioner four times in the last year. Of these 21 patients, 17 declared they 'couldn't be better', two had 'mild' symptoms, one had 'moderate' symptoms and one 'couldn't be worse'.

FIGURE

*Relative drug usage*




*S.R.T. = sustained release tablet.

Salbutamol inhaler was the most common drug used by 50 patients (41%), followed by sodium chromoglycate (18.0%) and beclomethasone inhaler 22 (18.0%) (Fig). Sixteen patients (13.1%) considered themselves to have had 24 or more troublesome attacks in the last year and we assessed these to be in the moderate and severe categories. (Table I). Eleven of these patients were taking bronchodilators, sodium chromoglycate and/or inhaled or oral steroids. The remaining five patients were on either oral, inhaled or nebulised salbutamol, used as required. Two of these five had continuous symptoms with 30 and 40 attacks in the last year. Both had only attended the general practitioner once in that year.

Twenty patients (16.4%) had had at least one course of oral steroids or an increase in steroids in the last year, the average length of a course being one week. Seven of these patients were on continuous oral steroids. Of the 13 who had had at least one course of oral steroids, nine were taking bronchodilators, sodium chromoglycate and/or inhaled steroids, the remaining four were taking only bronchodilators. One would question if this is adequate prophylaxis. The

latter group included a 26-year-old who had frequent episodic symptoms and required salbutamol ten times per day. She had attended the general practitioner twice in the last year and had had 12 significant attacks in this time.

Twelve patients (9.8%) had been admitted to hospital in the last year, three of whom had two admissions. Eight of these patients were on bronchodilators, sodium chromoglycate and/or inhaled steroids. Of the remaining four, three were children under seven years who were managed on oral or nebulised bronchodilators and one was a 49-year-old male who had had two admissions in the last year and was treated with short courses of steroids. He complained of continuous cough and frequent episodic wheeze and dyspnoea, yet had attended his general practitioner only once and was on salbutamol inhaler as required! Twenty-two patients (18.0%) had at some time been followed up in the hospital outpatient department for asthma. Twelve (9.8%) had obtained direct hospital admission without contacting their general practitioner.

Peak flow rate was monitored at each attack in 17 patients (13.9%), irregularly in 40 (37.8%) and never in 43 (35.2%). It was not practical in 22 (18.0%). Of the 43 patients who had never had a peak flow rate measured, only three had a single vitalograph reading and this was to demonstrate reversibility. Five out of the 16 patients who had had 24 or more significant acute attacks in one year had regular monitoring, eight had irregular monitoring, two had none, and monitoring was not practical in one case. Of the 20 patients who took oral steroids intermittently or continuously, only five had regular monitoring, eight had irregular monitoring, five had none, and with two it was not practical. Of the five patients who had never had peak flow monitoring, one was on continuous oral steroids. Twenty-six patients (21.3%) had vitalograph measurements carried out, which were mainly used for diagnostic purposes to demonstrate reversibility.

## DISCUSSION

This audit of asthma patients is an example of the use of a microcomputer in practice to identify patients. One hundred and twenty-two asthmatics (3.9%) were identified in a practice of 3140 patients. Thirteen different diagnostic labels were used with up to five different labels used for a single patient. This indicates difficulty in labelling the asthmatic and some labels may have been chosen to avoid alarming the patient by the term 'asthma'. However, this can only lead to confusion and possible undertreatment, particularly in a group practice of several general practitioners. With good education and treatment, patients can only benefit from knowing their diagnosis.

Inadequate use of prophylactic therapy (inhaled steroids, regular use of bronchodilators and sodium chromoglycate) has been confirmed, and the study shows that this is not always the doctor's fault but can sometimes be attributed to lack of patient compliance.

Shee et al[3] and the British Thoracic Association in its study of 90 asthmatic deaths,[2] also found asthmatics inadequately treated and this again not only due to poor doctor management: some patients ignored their asthma. The British Thoracic Association found that only 47 per cent of patients co-operated fully in their treatment and they found patients with severe symptoms who repeatedly failed to renew prescriptions or to visit the doctor as requested. Does this failure of the patient reflect a lack of knowledge about asthma? Or is it due to a wish to ignore or forget their illness; or a fear of possible side- effects from their drugs, as found by Harding and Modell?[4]

The British Thoracic Association also found that deaths were more likely in those with chronic persistent symptoms, or those who had had previous sudden or severe attacks and unstable patterns with variable peak flow rates. Delay in starting treatment was the single most important factor, due mostly to the patient not recognising the severity of the attack. In the present study inadequate monitoring using the peak flow meter and vitalograph was found. While the condition of the patient can be assessed clinically to some degree from the history and physical examination, an objective test is highly desirable.[5] The peak flow meter gives the doctor a simple tool with which he can assess the patient's condition and the effectiveness of therapy.[6]

In well-motivated patients, peak flow rates could be used to monitor the patient's day-to-day condition at home, so that impending attacks can be treated before full development has occurred, as with diabetic patients who monitor their blood sugars. This, with clear guidelines, could overcome some of the problems that patients have in deciding when to seek help.

In conclusion, many asthmatics are receiving inadequate treatment due to both patient and doctor failure, with poor monitoring of their condition. Better use of inhalers, with regular peak flow rate monitoring by the general practitioner and possibly home monitoring by the patient, patient diaries and better patient education, may go some way in reducing asthma deaths and improving morbidity.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 165 – 170, October 1985.

# Gastro-oesophageal reflux – initial experience with a radiotelemetry system for prolonged oesophageal pH monitoring

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Accepted 15th August 1985.


## SUMMARY

*A radiotelemetry system has been used to monitor gastro-oesophageal reflux over a prolonged period in 27 asymptomatic control subjects and in 15 patients with reflux symptoms. In control subjects, the frequency of reflux episodes (pH < 5) ranged from 0.1 – 0.7 per hour of recording (median 0.36) by day, and from 0 – 1.0 per hour (median 0.12) by night. The duration of reflux (pH < 5) per hour of recording ranged from 0.4 – 5.4 minutes (median 2.1) by day and from 0 – 5.1 minutes (median 0.27) by night. Patients with reflux symptoms had more frequent episodes of daytime reflux and a longer duration of daytime reflux than control subjects. The frequency and duration of nocturnal reflux were similar in patients and in control subjects. Of two patients with Barrett's metaplasia of the lower oesophagus, one had markedly increased frequency and duration of both daytime and nocturnal acid reflux, while the other had only a moderate increase in the frequency of daytime reflux episodes.*


## INTRODUCTION

Reflux oesophagitis is one of the commonest conditions encountered in clinical practice. Although fibreoptic endoscopy greatly assists in the diagnosis, it provides an assessment only of the extent of oesophageal mucosal damage and gives no indication of the severity of gastro-oesophageal reflux.

Prolonged intra-oesophageal pH monitoring has been developed so that a quantitative assessment of gastro-oesophageal reflux may be made. Early studies used a small glass pH electrode which was connected to a large bedside pH recording device.[1-3] Patients were rendered relatively immobile by the apparatus and the relevance of the reflux patterns obtained was questioned. A major advance has been the refinement of a radiotelemetry system for pH monitoring so that fully ambulatory studies of oesophageal pH are now feasible.[4]

We present our initial experience with this new technique and describe the pattern of gastro-oesophageal reflux in a group of asymptomatic healthy human volunteers and in a group of patients with symptoms of gastro-oesophageal reflux.

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## METHODS

A pH sensitive radiotelemetry capsule emits a radio signal which alters according to the pH of the surrounding environment. The signal is then detected by a portable radio-receiver and stored on a 24-hour cassette tape. The radiotelemetry capsule (model 7006 Rigel Research) consists of a glass envelope (28.0 x 6.6 mm) and is similar in size to an antibiotic capsule. The envelope contains a glass electrode, a radio-transmitter, a small mercury battery and a self-contained reference cell measuring pH in the range 1 to 9. The capsule is attached to a 40 cm length of fine bore polyvinyl tubing (OD = 0.54 mm).

Before it was swallowed by each patient or volunteer, the capsule was calibrated at pH 4.0, 7.0 and 9.0 at 37°C. When the capsule was swallowed, the upper end of the polyvinyl tubing was taped to the patient's cheek, so that the capsule was maintained in the oesophagus 5 cm above the oesophago-gastric junction. The distance from mouth to oesophago-gastric junction was recorded during previous endoscopy or manometric studies. The capsule was re-calibrated at the end of each study to check pH 'drift' during the test.

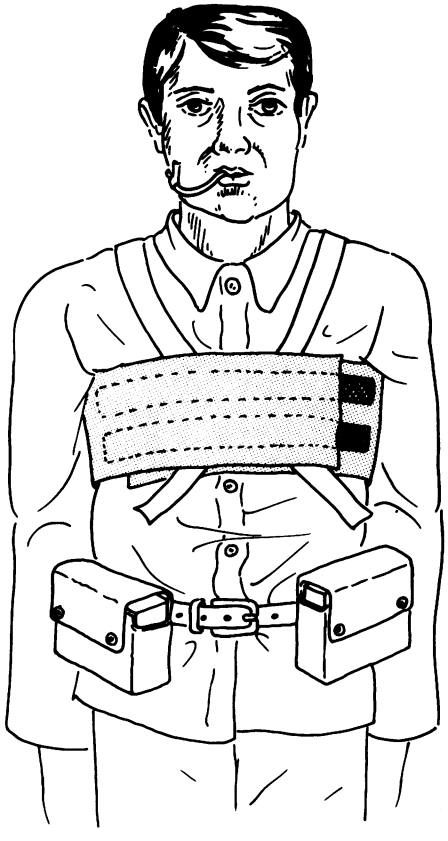

Fig 1. The portable receiving and recording system for oesophageal pH monitoring.

A compact portable receiving and recording system was used for pH monitoring (Fig 1). This consisted of a battery-operated FM radio receiver and aerial switching unit which recorded on to a Medilog four-channel cassette recorder (Oxford Medical Systems). An aerial belt, worn across the chest, was used to detect the signal from the radiotelemetry capsule. Signals recorded on the 24-hour tape cassette were replayed on a Devices MX4 unit so that a graphical record of each patient's reflux pattern was obtained (Fig 2). The apparatus included an event button which patients could press if they

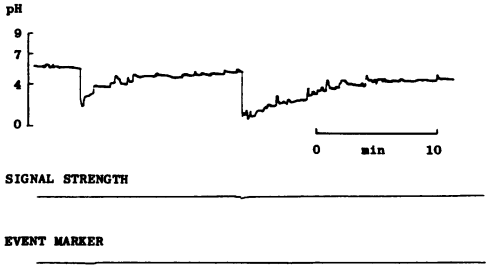


Fig 2. Graphical record showing two reflux episodes. The sudden fall in pH represents gastro-oesophageal reflux. The continuous line for signal strength shows persistence of an adequate signal from the capsule. The absence of the sensation of heartburn during these two episodes is shown by no 'blip' on the manually-operated event marker.

experienced the sensation of heartburn. All studies were conducted during an overnight hospital stay. Subjects were fully mobile but activity was standardised to allow comparison between different groups. Food and drink of pH $< 5$ were excluded from the hospital diet. The radiotelemetry capsule was inserted at approximately 3.30 pm and removed at 9.00 am the following morning so that 17-18 hours of recording were available for analysis.

Acid reflux episodes were arbitrarily defined at two levels — when the oesophageal pH fell from the normal value of 7 to less than 5 pH units or when it fell further to less than 4 pH units. These two levels are necessary because there is no simultaneous measure in these patients of gastric juice pH which may rise to between 4 and 5 pH units in the postprandial period. The duration of reflux (minutes per recorded hour) and the number of reflux episodes per recorded hour were determined. Reflux data for daytime and for night-time were analysed separately. Inter-group comparisons were made using the non-parametric Mann-Whitney-U test. The upper limit of the normal range for reflux frequency or duration was defined as the 95th centile, since the data were not normally distributed.

## PATIENTS

Group 1 consisted of 28 asymptomatic healthy volunteers, (14 men, 14 women) whose ages ranged from 20 to 63 years (mean age 36 years). No volunteer was taking medication likely to influence gastrointestinal motility nor gave a history of gastro-oesophageal reflux symptoms.

Group 2 consisted of 15 patients (7 men, 8 women) whose ages ranged from 21 to 63 years and who presented with symptoms of heartburn. In some cases, regurgitation or dysphagia was also present. Endoscopy was performed in all cases, and significant erosive oesophagitis was noted in 10 patients, two of whom (males, aged 36 and 38 years) had associated Barrett's metaplasia in the lower 5-10 cm of oesophagus. In five patients the oesophagus appeared normal or had mild erythema only. No patient was taking any medication other than simple antacids prior to the study, and no antacids were supplied during the pH monitoring study.

## RESULTS

Most patients and volunteers experienced little difficulty in swallowing the radiotelemetry capsule. One control subject retched at frequent intervals and rejected the capsule after only 1½ hours. Her recording was not included in the analysis of data. One patient tolerated the capsule well until 11 pm, at which time she regurgitated the capsule and was reluctant to swallow it again. Eight hours of daytime recording were obtained from this patient. With the capsule *in situ,* all patients and volunteers were fully mobile and, thus, the aim of ambulatory monitoring was achieved. Some individuals experienced difficulty in eating food during the study.

Acid reflux was detected in all asymptomatic volunteers and yet no volunteer complained of heartburn during the study. The Table shows that most reflux episodes occurred by day when volunteers were upright, and of these episodes most were observed to occur post-prandially. Nocturnal reflux was an infrequent phenomenon and did not occur at all in several individuals.

Patients with reflux symptoms had more frequent episodes of daytime reflux than asymptomatic control subjects ($p < 0.001$) (Fig 3). The time of oesophageal

TABLE

*Frequency and duration of gastro-oesophageal reflux episodes in 27 control subjects*

| | Frequency (episodes / hour) | | Duration (minutes / hour) | |
|---|---|---|---|---|
| | Day | Night | Day | Night |
| pH < 5 | | | | |
| Median | 0.4 | 0.1 | 2.1 | 0.3 |
| Range | 0.1 – 0.7 | 0 – 1.0 | 0.4 – 5.4 | 0 – 5.1 |
| 95th Centile | 0.6 | 0.4 | 5.0 | 2.3 |
| pH < 4 | | | | |
| Median | 0.3 | 0.11 | 1.73 | 0.15 |
| Range | 0.1 – 0.7 | 0 – 0.9 | 0.3 – 3.8 | 0 – 4.4 |
| 95th Centile | 0.6 | 0.3 | 3.2 | 1.9 |

exposure to pH < 5 during the daytime was significantly longer in the patient group than in the control subjects ($p < 0.01$) (Fig 3). Although the duration at pH < 4 by day tended to be longer in the patient group, this did not reach statistical significance ($p = 0.18$). The frequency and duration of nocturnal reflux were similar in the patient group and in the control group, no statistically significant differences being detected.

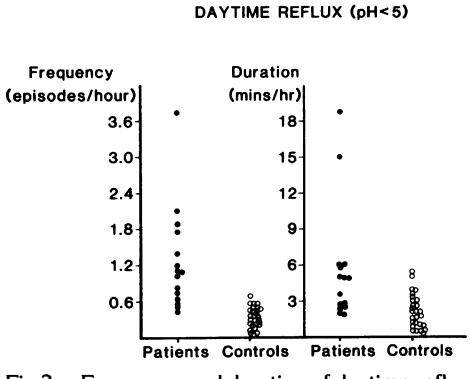


Fig 3. Frequency and duration of daytime reflux episodes in 15 patients with reflux symptoms and in 27 control subjects.

One of the two patients with Barrett's oesophageal metaplasia had grossly abnormal daytime reflux (18.9 min/hr at pH < 5) and nocturnal reflux (4.3 min/hr at pH < 5), whereas the other patient had no nocturnal reflux detected, a normal duration of daytime reflux (2.9 min/hr at pH < 5) and a moderate increase in the frequency of daytime reflux episodes (1.2 episodes of pH < 5/hr).

More severe reflux tended to occur in the 10 patients with significant erosive oesophagitis than in the five patients with minimal change or normal appearance. Overlap between these groups was noted and formal statistical evaluation was not applied in view of the small number in the second group. Only four of the reflux patients had evidence of abnormal nocturnal reflux and all four had significant erosive oesophagitis.

## DISCUSSION

Our data illustrate clearly that gastro-oesophageal reflux occurs in asymptomatic volunteers. Other investigators have described similar findings in control subjects[2] who were confined to bed and in ambulatory subjects.[5] However, those studies

were based on smaller numbers of volunteers who were mostly young adults. We have examined reflux patterns in healthy men and women of a wider age group and our control values for reflux are more broadly based for comparison with different patient groups.

The normal occurrence of gastro-oesophageal reflux when upright, by day, has been highlighted in this study and most episodes were observed post-prandially. Clearly, gravity and the supine position exert little influence on the competence of the lower oesophageal sphincter. After a meal, however, several factors, including the intra-gastric pressure and volume, and the release of gastro-intestinal hormones, may modify lower oesophageal sphincter tone and promote gastro-oesophageal reflux.[6] Continuous pressure recordings have recently documented the occurrence of transient, inappropriate relaxations of the lower oesophageal sphincter post-prandially[7] and further studies are required to elucidate the mechanism of this phenomenon.

Studies of acidity in patients with reflux symptoms have given an insight into the varying patterns of abnormal gastro-oesophageal reflux and have raised many questions about the nature of this disorder. DeMeester and colleagues emphasised the importance of supine, nocturnal reflux in patients with severe oesophageal mucosal damage.[8] However, our own observations and those of Branicki and colleagues[5] suggest that excessive nocturnal reflux occurs in a relatively small sub-group of patients with significant oesophagitis. The time-honoured practice of advising patients to raise the head of the bed is unlikely to benefit the majority of patients with reflux symptoms.

Our data have highlighted the occurrence of frequent short episodes of reflux in some individuals with reflux symptoms and fewer episodes of much longer duration in other patients. As more patients are studied in the coming years, it is hoped that the significance of these differing reflux patterns can be determined. Some of our patients with erosive oesophagitis had normal or only mildly abnormal reflux patterns. There are several possible explanations for this observation. Reflux may not be responsible for the problem and a different mucosal damaging agent may be involved, such as a viral illness or a mucosal irritant in the diet. Severe duodenogastric reflux may occur in some individuals so that bile contaminated gastric juice which is no longer acidic may be refluxing into the oesophagus.[9]

Our observations on the two patients with Barrett's oesophageal metaplasia fuel the controversy about the aetiology of this disorder. The current hypothesis is that these patients develop a metaplastic change in the oesophagus as a consequence of severe, prolonged gastro-oesophageal reflux.[10] Barrett believed that the condition was the result of a failure of the embryonic lining of the oesophagus to achieve normal maturity.[11] One of our patients had grossly abnormal daytime and nocturnal gastro-oesophageal reflux, whereas the other had no nocturnal reflux at all and his daytime reflux was only mildly increased.

It is clear that prolonged oesophageal pH monitoring is an important research tool which gives invaluable information about the pathophysiology of reflux oesophagitis. It also has many applications in clinical practice. The effectiveness of anti-reflux surgery and of current medical therapy on the severity of gastro-oesophageal reflux can be readily assessed. New drug treatments can be examined. Diagnostic problems may be solved with the technique. Some patients have atypical symptoms such as cough, wheezing[12] and chest pain[13] which are

secondary to gastro-oesophageal reflux, and pH monitoring may assist the assessment of such individuals. The contribution of reflux to the collection of symptoms associated with gallbladder disease and peptic ulcer may also be unravelled by this investigation.

The radiotelemetry system of pH monitoring has proved accurate and reliable in our hands, and patient tolerance has been good. Our subjects have been studied under hospital conditions to allow inter-group comparisons, but the apparatus could be used in the home or at work so that environmental factors peculiar to each individual can make their contribution to the degree of gastro-oesophageal reflux detected with the equipment.

We thank Janssen Pharmaceuticals Ltd. who gave financial support to this investigation. Sister E. Crawford assisted with oesophageal pH and manometry studies.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 171 – 175, October 1985.*

# Immediate coronary care in general practice — a three-year review

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Accepted 15th August 1985.


## SUMMARY

*The general practitioners in a rural practice in a three-year period were called to 101 patients (25% female) who suffered a myocardial infarction. The average response time was 15 minutes. Seventeen patients collapsed and died and the 84 who survived the initial period were given immediate coronary care and either cared for at home, admitted by cardiac ambulance to a coronary care unit, or admitted to a general medical ward with monitor facilities. The four-week mortality rates were 21.0%, 21.5% and 57.7% respectively. Thirty-six patients required treatment for arrhythmias in the initial care period, of whom nine required defibrillation. This survey supports the view that patients over the age of 60 years with uncomplicated myocardial infarction may be cared for successfully at home.*


## INTRODUCTION

Ischaemic heart disease is the commonest single cause of death in the United Kingdom, and an estimated 150,000 people die each year from coronary heart disease. It has been recognised for many years that deaths following myocardial infarction are greatest in the first two hours and that 90% of these deaths are caused by ventricular fibrillation, a condition which is reversible when treated early.[1] The general practitioner, particularly in the country areas, is well placed to have a direct influence on the morbidity and mortality rates of his patients following a myocardial infarction by providing immediate coronary care.

'Immediate care' may be defined as the provision of early comprehensive medical care by a skilled practitioner with appropriate equipment. The aims of this immediate care in the patient with an acute myocardial infarction are: (1) To prevent early death due to ventricular arrhythmias; and (2) To limit the size of the myocardial infarct by maximising and maintaining the coronary artery perfusion.

## EQUIPMENT AND ORGANISATION

The equipment for general practice coronary care should be compact and easily portable. We were fortunate in this respect, because resuscitation equipment was already in use in the practice and was suitable for treating cases of cardiac arrest. An electrocardiogram had also been part of the practice equipment for the past ten years; this was easily portable and was suitable for use in a patient's home. Three further items of equipment were required to complete the coronary kit. A battery-powered cardiac monitor, a Pantridge defibrillator, and a lightweight

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plastic 'implement box' were purchased. This box gave excellent access to drugs, syringes, needles, venous access cannulas and the monitor. The equipment is normally kept in the Health Centre ready for immediate use during working hours. Out of hours it is carried in the car of the doctor on call, which is equipped with a two-way radio. The doctor also carries a pager in his pocket when he is out of his car.

A protocol for patient management was initially agreed to ensure a conformity of patient care. The request for medical aid for a patient with a history suspicious of myocardial infarction was treated by the doctor on call as an emergency and on arrival the monitor was immediately attached to the patient's chest in order to establish the cardiac rhythm. Pain was relieved as soon as possible and a venous access cannula inserted to give rapid access for intravenous drug administration. The cardiac rhythm was stabilised and heart failure, if present, was treated. A 12-lead electrocardiograph was recorded in all patients to assist in the diagnosis and for future reference. A blood sample for cardiac enzymes was taken from the patient who was to be cared for at home. Criteria were agreed by the doctors to assist in deciding which patients were suitable for home care: these were a stable cardiac rhythm, controlled pain, age greater than 70 years (or under 70 with an onset more than 2 hours previously), suitable home conditions and agreement of both patient and relatives. Each case was assessed on its merits. The age of patients suitable for home care was reduced from 70 to 60 years at the six months' review of the original protocol, when several patients in this age group had already insisted on home care and were having an uncomplicated convalescence.

## DRUG THERAPY

All drugs should be given intravenously, because the peripheral circulation is frequently impaired following myocardial infarction and this results in a slow absorption from an intramuscular injection site. Pain relief is obtained by giving diamorphine in sufficient quantity to relieve pain, normally 3 – 10 mg, the dose being titrated against the patient's response. The powdered diamorphine can be dissolved in cyclizine in order to control nausea and vomiting. Lignocaine in a dose of 50 – 100 mg given as a single injection, although not ideal, is the drug used at present to suppress ventricular ectopics or ventricular tachycardia. Sinus bradycardia (a rate under 50 beats/min) responds to atropine in doses of 0.3 – 0.9 mg and even in patients who have developed heart block will often increase the heart rate in the initial period. When bradycardia is due to prior treatment by beta blockade, no drug treatment is required except when hypotension (systolic BP $< 100$ mmHg) or ventricular ectopics occur. Ventricular ectopics occurring in a patient with bradycardia will frequently be eliminated as the heart rate increases.

Tachycardia (a rate excess of 110 beats/min) can be treated successfully with sotolol 5 – 10 mg or other beta-blocker, provided the tachycardia is not caused by left ventricular failure when a diuretic and possibly digoxin should be given first. The drug should be given slowly and titrated against the patient's response. Ventricular fibrillation is treated by direct current shock using a defibrillator. Prolonged ventricular fibrillation is associated with the development of acidosis which may be severe and requires intravenous bicarbonate. Sodium bicarbonate can conveniently be given in general practice by a pre-packed injection of 50 ml hypertonic sodium bicarbonate (50 mmol/50 ml). Sustained ventricular tachy-

cardia which fails to respond to the injection of 100 mg lignocaine, especially when accompanied by a falling blood pressure, may require an unsynchronised direct current shock and intravenous bicarbonate.

## RESULTS

A proforma was filled in by the attending doctor following each case; this was completed after 28 days or earlier if the patient died. One hundred and one patients (25% of whom were female) were attended in this series (Figure). Eleven patients were found to be dead on the doctor's arrival. Six others were severely shocked with marked cyanosis and systolic blood pressure less than 50 mmHg, all of whom failed to respond to treatment, and death followed within minutes from ventricular fibrillation and asystole. Cardiopulmonary resuscitation and defibrillating shocks were unsuccessful. Early deaths occurred in 17% of patients.

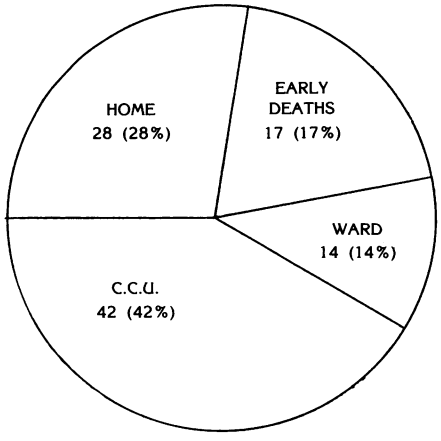


Figure. Management of 101 patients with myocardial infarction (1980 – 1983).

The age of patients ranged from 38 to 92 years with the most commonly affected group being 60 – 80 years. Eighty-four patients survived the initial period. Forty-two patients were transported by cardiac ambulance to a coronary care unit, nine of whom died, resulting in a mortality rate of 21.5 per cent. Fourteen patients with uncomplicated infarcts were admitted to a general medical ward, eight of whom died, a mortality rate of 57.7 per cent. Twenty-eight patients were treated at home with an age range of 59 to 92 years. Six of this group had to be subsequently transferred to a coronary care unit, four because of recurrence of chest pain (three due to a further ischaemic episode and one to pericardial involvement) and two because of change in home circumstances. Two of the transferred patients died in hospital and a further four of the group died at home, resulting in a mortality rate of 21 per cent. (Table I).

TABLE I

*Mortality rate by place of care*

| | *Patients* | *Deaths* | *Mortality* |
|---|---|---|---|
| Coronary care unit | 42 | 9 | 21.5% |
| Home | 28 | 6 | 21.0% |
| General ward | 14 | 8 | 57.7% |

Patients aged from 60 to 79 years proved the most suitable groups for comparison and if patients with early complications were excluded (ie ventricular arrhythmias and cardiac failures) mortality rates of 20% and 19.1% were found for coronary care unit and home care. (Table II).

TABLE II

*Mortality rate — age adjusted*
*(Patients 60 – 79 years, excluding those with early complications)*

| *Place of care* | *No.* | *Mortality rate* |
|---|---|---|
| CCU | 20 | 20.0% (4) |
| Home | 21 | 19.1% (4) |

Analysis of the 17 patients who died early showed that 11 of them (70.6 per cent), eight of whom had no previous history of heart disease, suffered a sudden collapse. Five of the six patients presenting with cardiogenic shock had a history of a previous myocardial infarction. The arrhythmias requiring treatment in the immediate care period (the initial period when under the care of the general practitioner before removal to hospital or before the general practitioner left the patient) were determined in 36 (36 per cent) of patients. Bradycardia was the commonest arrhythmia (14 per cent), with ventricular ectopics recorded in 4%. Ventricular fibrillation presented in nine patients (9 per cent), six of whom presented with cardiogenic shock. (Table III). Cardiac output was re-established in four of these and two patients survived longer than four weeks, giving a survival rate of 22 per cent. This compares with a published Belfast figure of 26 per cent.[2]

TABLE III

*Early arrhythmias*

| | | |
|---|---|---|
| Bradycardia | 14 | (14%) |
| Ventricular fibrillation | 9 | ( 9%) |
| Tachycardia | 5 | ( 5%) |
| Multiple ventricular ectopics | 4 | ( 4%) |
| Atrial fibrillation | 4 | ( 4%) |

## DISCUSSION

The doctor's average response time, from receiving the call to arriving with the patient, over the three-year period was fifteen minutes. The mortality rate in the first four weeks for all myocardial infarctions in the practice area in the three-year period was 50 per cent. This is in line with the recent study of Wilson et al (1983)[3] which compares two community mortality rates in the North of Ireland — one area served by cardiac ambulance and coronary care unit had a mortality rate of 47%, and the area not thus served had a mortality rate of 60%.

This survey supports the view that patients over the age of 60 years with uncomplicated myocardial infarctions have as good a chance of survival if they are cared for at home, provided pain is relieved and cardiac condition stabilised. The delay in request for medical aid still exceeds one hour on average, except in the group of patients who suffer from a sudden collapse. Many patients, if given the choice, would prefer home care to hospital care and there are also economic reasons for keeping patients out of hospital. The general practitioner has much to gain by providing high quality care both in the patients' estimation of his care and in his own self-esteem.

General practice coronary care has an important part to play in the management of myocardial infarction, particularly in the areas not served by mobile coronary care and coronary care unit. This survey supports the view that patients with uncomplicated myocardial infarctions have as good a chance of long-term survival if cared for at home as in the coronary care unit.

I would like to thank my partners for their fortitude and attention to detail during the three years of the survey.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 176 – 180, October 1985.*

# Thymectomy for myasthenia gravis

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Accepted 17th July 1985.

## SUMMARY

*The results of 14 years' experience in the surgical treatment of myasthenia gravis are reported. Twenty-one patients (14 female, 7 male) underwent thymectomy for myasthenia gravis between 1971 and 1984. The mean age of the patients was 33 years (range 14 – 57 years). The median duration of symptoms prior to surgery was 18 months (range 5 months to 35 years). The mean follow-up was 5.3 years. There were no post-operative deaths: 76% obtained benefit from thymectomy. The patients' age, sex, duration of symptoms and histology of the thymus gland did not correlate with the result of treatment. This series suggests that, while thymectomy is often beneficial in the treatment of myasthenia gravis, there are no accurate predictors of the outcome following surgery.*

## INTRODUCTION

Myasthenia gravis is an uncommon disease characterised by a fluctuating course and occasional spontaneous remissions. The association between this disease and thymic pathology has long been recognised.[1] Since the results of thymectomies were first reported, over forty years ago,[2] surgery has played an increasingly important role in its management. While there is general agreement about the potential benefits of operative intervention,[3] there has been considerable debate about the indications for timing of surgery, and also the prediction of its results. The high morbidity and mortality quoted in earlier series,[2, 4] together with reports that young women with mild disease of short duration were more likely to do better,[5] tended to influence patient selection. As a result, a fair assessment of thymectomy was not possible. More recent series have broadened patient selection considerably,[6, 7, 8] yet reported benefits have remained high. Prediction of the outcome in the individual case remains an area of disagreement.[6, 7] The purpose of this paper is to review our experience in the surgical treatment of myasthenia gravis and to determine whether it is possible to predict the results of treatment.

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## PATIENTS

It has been the practice in the Neurology Department in this hospital to refer only those patients with the generalised and bulbar forms of the disease. Traditionally, those of sixty years of age or older, and those with the purely ocular forms of the disease, have not been referred. In view of these selection criteria, we estimate that approximately 80% of myasthenics in this hospital have come to surgery.

From November 1971 to February 1984, 21 patients (14 female, 7 male) with myasthenia gravis were referred to the Department of Thoracic Surgery for thymectomy. (Table I). Prior to referral, the diagnosis had been established by a consultant neurologist. The age of patients at the time of surgery ranged from 14 to 57 years (mean of 33 years). The mean age of the females was less than that of the males: 29.2 and 41.1 years respectively. The duration of symptoms prior to thymectomy ranged from 5 months to 35 years (median of 18 months). Standard anti-cholinesterase therapy was continued up until the night before surgery and recommenced immediately afterwards. All underwent a total thymectomy via a median sternotomy. All patients have been assessed post-operatively at regular intervals by a consultant neurologist. The period of review following surgery ranged from 6 months to 12 years, with a mean of 5.3 years.

TABLE I

*Patients who underwent thymectomy*

| *Patient* | *Age* | *Sex* | *Duration of symptoms (months)* | *Type of disease* | *Histology of the thymus* | *Length of follow-up (months)* | *Outcome* |
|---|---|---|---|---|---|---|---|
| DI | 24 | M | 24 | Bulbar | Hyperplasia | 6 | Moderate benefit |
| NE | 57 | M | 6 | General | Normal | 48 | Considerable benefit |
| JK | 22 | F | 48 | General | Hyperplasia | 132 | Considerable benefit |
| RC | 48 | M | 12 | Bulbar | Thymoma | 78 | Moderate benefit |
| NK | 25 | F | 10 | General | Hyperplasia | 60 | Considerable benefit |
| MC | 57 | F | 420 | General | Normal | 12 | Moderate benefit |
| NB | 42 | M | 26 | General | Normal | 132 | Moderate benefit |
| ID | 27 | F | 72 | General | Hyperplasia | 6 | Considerable benefit |
| RD | 36 | M | 10 | General | Thymoma | 48 | Considerable benefit |
| AG | 18 | F | 11 | General | Hyperplasia | 18 | Considerable benefit |
| BO'H | 14 | F | 5 | General | Hyperplasia | 84 | Considerable benefit |
| MF | 16 | F | 10 | General | Hyperplasia | 6 | Moderate benefit |
| MB | 23 | F | 18 | General | Normal | 72 | No benefit |
| OMcG | 21 | F | 12 | General | Thymoma | 48 | No benefit |
| NMcM | 41 | F | 21 | General | Normal | 24 | No benefit |
| JW | 34 | M | 5 | Bulbar | Thymoma | 108 | No benefit |
| EC | 47 | M | 18 | Bulbar | Thymoma | 96 | Worse |
| AF | 53 | F | 14 | Bulbar | Thymoma | 72 | Remission |
| MH | 18 | F | 30 | General | Normal | 144 | Remission |
| AG | 29 | F | 60 | General | Normal | 72 | Remission |
| PM | 45 | F | 78 | Bulbar | Normal | 72 | Remission |

## RESULTS

The patients were divided into four groups:

1 — patients in remission with no symptoms and no therapy.
2 — those who had obtained considerable benefit with only mild symptoms remaining but still on some therapy.

3 — those who had obtained moderate benefit with drug dosage of about half the pre-operative amount.

4 — those who obtained no benefit or were worse off following surgery, needing either the same or additional therapy.

Only 4 patients achieved complete remission (19%), all of whom were women. Overall 16 (76%) benefited from thymectomy (Table II). There was no difference in benefit between the sexes. Five achieved no benefit or were worse off following surgery (24%). There were no post-operative deaths or deaths at a later period. Five of the group of 21 patients required ventilatory support for periods ranging from 5 days to one month post-operatively.

TABLE II

*Outcome following surgery*

| *Group* | *No.* | *Per cent* | |
|---|---|---|---|
| 1. Remission | 4 | 19 | 76 |
| 2. Considerable benefit | 7 | 33 | |
| 3. Moderate benefit | 5 | 24 | |
| 4. No benefit or worse | 5 | 24 | |

The most common pathological findings were hyperplasia (7 cases), thymoma (6 cases) and normal glands (8 cases). There appeared to be no correlation between thymic pathology and the surgical result. There was no difference in age between those who benefited from thymectomy and those who did not (mean 34.0 and 33.2 years respectively). There was no difference between the median duration of symptoms (benefit 19 months, no benefit 18 months) or in the sex distribution (benefit 79% female, 71% male). (Table III).

TABLE III

*Relationship of outcome to pre-operative details and histology*

| *Group* | *Sex* | *Mean age (years)* | *Median duration of symptoms (months)* | *Type of disease*[1] | *Histology*[2] |
|---|---|---|---|---|---|
| 1. Remission | 4F | 36.3 | 45 | 2G, 2B | 3N, 1T |
| 2. Considerable benefit | 5F, 2M | 28.4 | 11 | 7G | 1T, 1N, 5H |
| 3. Moderate benefit | 2F, 3M | 37.4 | 24 | 3G, 2B | 1T, 2N, 2H |
| 4. No benefit or worse | 3F, 2M | 33.2 | 18 | 3G, 2B | 2N, 3T |

(1) G = generalised, B = bulbar.

(2) N = normal, T = thymoma, H = hyperplasia.

## DISCUSSION

When Blalock reported the results of the first series of thymectomies for myasthenia gravis 40 years ago, he concluded that, while the procedure was probably beneficial, it was not possible to predict the outcome of surgery.[2]

Since then, there has been unanimous agreement that thymectomy can be of benefit but considerable disagreement on the prediction of results. Five years after this first series, Keynes reported that a long history prior to surgery was prejudicial to recovery.[9] He also made the important observation that, due to the fluctuating course of the disease, it was difficult to assess the results. In an extensive review of Keynes's work, Simpson in 1958 reaffirmed the conclusion that those most likely to benefit from surgery were those with symptoms of less than five years' duration.[1] Apart from this, no other significant factors were observed which could help predict the outcome.

While there are still those who feel that young women[6, 11] and those patients having a short history[6, 10] constitute favourable groupings, there is considerable evidence from others that there are no reliable predictors of a favourable result.[3, 7] Attempts have been made to correlate thymic pathology[9, 14] and acetylcholine receptor antibody titres[13, 14] with the results of surgery. However, recent reports suggest that, with the exception of thymomas which may indicate a poor prognosis, pathological findings[6, 7, 15, 16] and reduction in acetylcholine receptor antibody titres[11, 12, 16] are not important factors in the outcome following thymectomy.

From this series we can make several observations. With 76% obtaining benefit from thymectomy there can be no doubt that it is a worthwhile procedure. There was no sex difference between those who improved following surgery and those who did not, but it is worth noting that all those who obtained a complete remission were female. We could find no evidence that age or short duration of symptoms were favourable factors, in fact one patient with symptoms for 35 years benefited from surgery. Neither did thymic histology seem to correlate with the eventual outcome, two patients with thymomas responding well to surgery. That there is a very definite morbidity associated with thymectomy in those suffering from myasthenia gravis[17] is borne out by five out of our group of 21 requiring post-operative ventilatory support. Unlike some of the earlier series which reported a high mortality,[2, 4] we had no deaths in the immediate post-operative period or later during the period of this review.

In conclusion we feel that thymectomy is a relatively safe and effective procedure in the management of myasthenia gravis. From our experience there are no factors which enable one to predict the outcome of surgery. For this reason we feel that surgery should be offered to all except those with the mildest disease.

The authors would like to thank Dr M W Swallow, Dr J A Lyttle and Dr S A Hawkins from the Department of Neurology, RVH, for permission to review the records of patients under their care, and the staff of the Department of Pathology, RVH, for histological examination of the thymus glands.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 181 – 184, October 1985.*

# A review of referrals to the psychosexual clinic at the Belfast City Hospital

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Accepted 1st September 1985.


## SUMMARY

*The number of patients seen at the psychosexual clinic has more than doubled in eight years. The diagnostic categories of the patients referred have also changed, especially in the area of homosexuality, and now show greater similarity to figures obtained in two reports from Great Britain, apart from a lower referral rate for orgasmic dysfunction. There is also an overall lower rate of referral in Northern Ireland. This raises the question as to whether or not there is a real difference in the prevalence of these disorders in the Province, compared with Great Britain.*


## INTRODUCTION

The psychosexual clinic has been in existence for approximately twelve years. It is part of the Department of Mental Health at the Belfast City Hospital. It investigates and treats a wide variety of sexual problems. The service is organised by a consultant psychiatrist who either sees the cases personally or supervises the work of others, who include psychiatrists in training, a general practitioner clinical assistant, a senior clinical psychologist, a social worker and a nurse therapist. Quinn et al[1] have described the service provided by this clinic. Since then, the number of patients seen and treated at the clinic has greatly increased. It seemed important to re-evaluate the referral patterns and the nature of the problems referred. All referrals in 1982 were studied with special reference to the referring agent. Because the majority of these came from general practitioners the report focusses particularly on this aspect.

## REFERRALS

In 1982, 206 cases were referred to the clinic from all areas of Northern Ireland (the population in the province in 1981 was 1,488,077, with an over-15 population of 1,097,653). The majority of these cases were referred either by their general practitioner or by psychiatrists working in other settings (See Table I). The remaining 21 cases were either self-referrals, or from social work departments or family planning clinics, and some cases were referred through the legal system.

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TABLE I

*Sources of referral*

| | | *No. of cases* | *Percentage* |
|---|---|---|---|
| General practitioner: | | 137 | 66.5 |
| Hospital: | | | |
| Psychiatrist | 18 | | |
| Physician | 12 | | |
| Gynaecologist | 10 | | |
| Surgeon | 7 | | |
| Radiotherapist | 1 | | |
| | | 48 | 23.3 |
| Others: | | 21 | 10.2 |
| TOTAL | | 206 | 100 |

Referrals from general practitioner principals in the four area boards are shown in Table II. A more detailed analysis of these referrals revealed a wider variation than was apparent between the individual boards, e.g. Newtownabbey and Lisburn showed the highest rate of referrals with seven doctors out of 27 in Newtownabbey referring (25.9%) and ten doctors out of 38 in Lisburn referring (26.3%); whereas there were no referrals at all in 1982 from Omagh and Larne/Carrickfergus, areas with 26 and 27 general practitioners respectively.

TABLE II

*Referrals from general practitioner principals in the four area boards*

| *Board* | *Total number of general practitioners* | *Number of referrals* | *Number of general practitioners referring* |
|---|---|---|---|
| Northern | 185 | 38 | 28 (15.1%) |
| Eastern | 370 | 70 | 57 (15.4%) |
| Southern | 155 | 16 | 16 (10.3%) |
| Western | 141 | 9 | 9 ( 6.4%) |
| TOTAL | 851 | 133 | 110 (12.9%) |

The diagnostic categories of the patients referred are shown in Table III. Erectile incompetence, premature ejaculation and retarded ejaculation were the dysfunctions most commonly seen in males, while general sexual dysfunction, orgasmic dysfunction and vaginismus were the female presenting conditions.

## DISCUSSION

A report on this clinic in 1974[1] showed that 92 cases were referred in the preceding year. The present survey shows that the figure had more than doubled by 1982. The rate of referral is much lower than that reported from Oxford[2] where 200 cases were seen in a 16-month period from an over-15 population of

TABLE III
*Diagnosis*

| *Dysfunction* | *Number of cases* | *Percentage* |
|---|---|---|
| MALE: | | |
| Erectile imcompetence | 56 | 27.2 |
| Premature ejaculation | 24 | 11.6 |
| Retarded ejaculation | 6 | 2.9 |
| FEMALE: | | |
| General sexual dysfunction | 52 | 25.2 |
| Orgasmic dysfunction | 5 | 2.4 |
| Vaginismus | 22 | 10.7 |
| OTHERS: | | |
| Homosexual | 10 | 4.7 |
| Exhibitionist | 7 | 3.6 |
| Sexual trauma | 7 | 3.5 |
| Others (including lesbians, paedophiles, trans-sexuals, transvestites, incest and fetish) | 17 | 8.2 |
| TOTAL | 206 | 100 |

219,000. A study from the Grampian region in Scotland[3] showed that out of all psychiatric referrals made in a two-year period for a population of 300,000 there were a hundred cases of sexual dysfunction, a referral rate approximately 25% higher.

Sixty-six per cent of cases were referred to the clinic by a general practitioner. This is similar to the 68.5% from the Oxford region. 12.9% of general practitioners in Northern Ireland referred patients in 1982. Comparing referrals from area boards it is apparent that fewer general practitioners referred from the Southern and Western Boards. This may well be related to the distance from the clinic; although it is interesting to note that 17.4% of general practitioners from the Coleraine – Ballymoney – Moyle area referred — a distance of approximately 60 miles from Belfast — while no general practitioners referred from the Larne/Carrickfergus area which is about 20 miles from Belfast. There may be other factors influencing a general practitioner's decision to refer. A survey carried out in 1974[4] to determine attitudes of British and Irish doctors to psychiatric referral asked how they would manage a case of sexual 'frigidity'; 14.2% in the Republic of Ireland and 14.1% in London said they would refer such a case to a psychiatrist, but the vast majority preferred to deal with it themselves or refer the patient to another individual or social agency.

There are other possible reasons for general practitioners not referring these patients, including the following, which were looked at in a paper on referrals to psychiatrists:[5] patients' dislike of referral to a psychiatrist, disadvantages of labelling, lack of readily available facilities, and delay in obtaining an appointment. Delay, which can be up to several months on occasions, may well be a significant deterrent to referral to this clinic. It has also been suggested[6] that resistance to referral may be influenced by a patient not wanting to re-describe an embarrassing

topic, or because sex therapy clinics are the subject of jokes, or because the patient feels that sex is an inappropriate topic to discuss. Cultural factors have also been suggested. These factors could apply to Northern Ireland, and embarrassment could prevent the patient presenting the problem to the general practitioner in the first instance. No information is available as to how general practitioners in Northern Ireland manage psychosexual disorders, though a survey is at present being undertaken. The increase in referrals in 1982 may be a reflection of the continued development of the psychosexual service in the province in the last ten years, or the inclusion of a course on human sexuality for undergraduate students,[7] or an increase in input in psychosexual medicine for postgraduate students and for doctors on in-service courses.

In 1982 the largest number of referrals were for erectile incompetence, and general sexual dysfunction. This was also the experience in Oxford and Grampian. There was a much lower referral rate for orgasmic dysfunction, 2.4%, in Belfast compared with 10% and 9% in Grampian and Oxford respectively. Vaginismus accounted for 10% of referrals in Belfast compared with 4% and 6% in Grampian and Oxford. Belfast still differs very considerably from the Oxford and Grampian regions in the diagnosis of orgasmic dysfunction. It is unclear why this is so. It may be due either to the under-diagnosis of the condition, or to hesitancy of presentation on the part of the patients.

Diagnostic categories in the Belfast study show one major change from 1974 when 22% of patients presenting were homosexual while they constitute only 4.7% of cases in 1982. This change brings the number of homosexuals seeking help more in line with the Oxford and Grampian regions. The reasons for this may be related to changing attitudes towards homosexuality and the setting up of a befriending organisation in Northern Ireland.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 185 – 190, October 1985.*

# The effect of oral alcohol on gastroenteropancreatic hormones in volunteers

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Accepted 10th June 1985.


## SUMMARY

*This study has examined changes in gastrointestinal hormones induced by alcohol. Ten normal volunteers consumed an orange and carbohydrate-containing drink on two separate occasions, with and without 50g alcohol. There was a significant hyperglycaemia associated with alcohol ingestion but no difference was noted in insulin or gastric inhibitory polypeptide in the two groups. Gastrin release was stimulated by alcohol but pancreatic polypeptide release and N-terminal glucagon release were both suppressed by alcohol. There was no difference in release of secretin or C-terminal glucagon in either group.*


## INTRODUCTION

Gastroenteropancreatic hormonal changes induced by alcohol may be responsible for many of the effects of alcohol, including gastritis, diarrhoea and abnormal carbohydrate metabolism.[1] The responses of gastroenteropancreatic hormones in normal subjects to oral alcohol are either unknown or in dispute.[1-9]

The aim of the study was to assess gastroenteropancreatic hormone changes induced by alcohol. Therefore we have studied normal volunteers who had oral alcohol in an orange and glucose drink. Assessment was made of serial alcohol, glucose and gastrointestinal hormones (insulin, gastrin, gastric inhibitory polypeptide (GIP), pancreatic polypeptide (PP), secretin and glucagon).

## PATIENTS AND METHODS

Normal fasting volunteers (six male and four female, mean age 22 years, range 18-34 years), with no history of diabetes mellitus or excess alcohol intake were included in the study. The project had the approval of the Royal Victoria Hospital Ethical Committee. Written informed consent was obtained from each volunteer.

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The experiment started at 9.00 a.m. when 10 volunteers (who were fasted from 10 p.m.) each had 50g 95% alcohol, diluted with 450 ml pure unsweetened orange juice containing 34g fructose, to which was added 34g glucose. Each volunteer was assessed on two mornings at least two weeks apart, having at random the drink with alcohol on one morning and without alcohol on the other morning. An indwelling cannula was inserted at time −15 minutes when an initial blood sample was taken for analysis. Blood samples were immediately transferred to chilled heparinised tubes and stored on ice prior to centrifugation. A second sample was taken at time zero and the volunteers were then given the orange drink which was consumed orally with blood samples at time 15, 30, 45, 60, 90, 120, 180 and 240 minutes. The cannula was flushed out after each sample with 0.5 ml physiological saline (0.9% Na Cl) and the first 3 ml of the venous sample were discarded to prevent contamination.

All samples were analysed for glucose and alcohol by colorimetry. Insulin, GIP, gastrin, N and C glucagon, secretin and PP were measured by radioimmunoassay.

Statistical analysis was performed using Wilcoxon matched-pairs signed-ranks test. Results are given ± standard error.

## RESULTS

Serum alcohol was increased to 2.4 mmol/l (± 0.4) after 15 minutes and reached a peak of 12.4 mmol/l (± 1.1) at 90 minutes. There was an overall elevation of serum glucose with alcohol with significantly higher glucose at 45 mins, 60 mins ($p < 0.01$) and 90 mins ($p < 0.05$) (Figs 1 and 2).

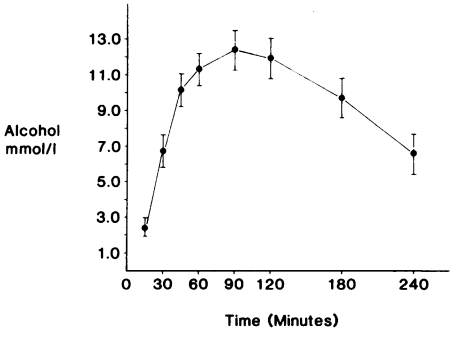


Fig 1. The change in serum alcohol (mmol/l) (± SEM) measured for 240 mins in 10 normal volunteers who each had 50g alcohol in an orange drink containing 34g fructose and 34g glucose

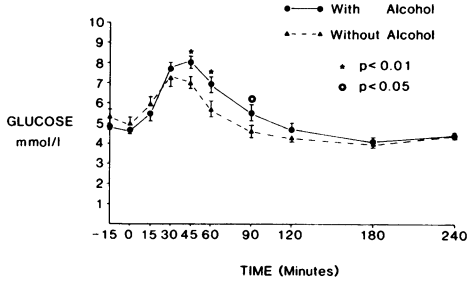


Fig 2. The change in serum glucose concentrations (mmol/l) (± SEM) in 10 normal volunteers measured over 240 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

Plasma insulin reached a peak of 74.7 mU/l (± 5.3) without alcohol and was suppressed with alcohol, reaching a peak of 59.0 mU/l (± 7.8) ($p < 0.05$) at 45 minutes. There was, however, no significant difference in the area under the curves, with or without alcohol. Plasma GIP was stimulated both with and without alcohol. There was no significant difference at any time and there was no overall difference in GIP release in the two groups assessed by the area under the curves (Figs 3 and 4).

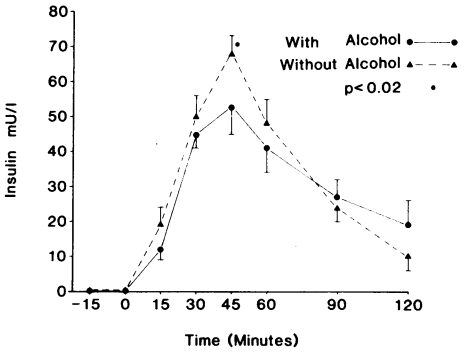


Fig 3. The change in plasma insulin concentrations (mU/l) ( ± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p value refers to 45 mins, comparing with and without alcohol).

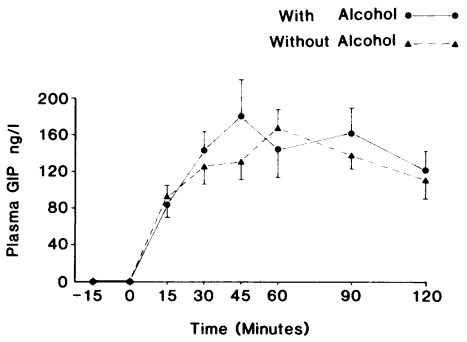


Fig 4. The change in plasma gastric inhibitory polypeptide (GIP) concentration ( ± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol.

Gastrin was stimulated with and without alcohol ($p < 0.001$), comparing peak values with baseline values. Alcohol produced further stimulation of gastrin release with significantly greater elevation of plasma gastrin at 45 and 90 minutes ($p < 0.05$), when compared with the controls without alcohol. The area under the gastrin curve with alcohol was 4129 ng/1/2h (± 821) and this was greater than the area under the curve without alcohol, 2019 ng/1/2h (± 367) ($p < 0.05$). There was no significant effect on secretin release with or without alcohol. N-terminal glucagon was stimulated by the orange drink without alcohol and was higher than with alcohol at times 45 minutes ($p < 0.005$), 90 minutes and 120 minutes ($p < 0.05$). The area under the curve without alcohol was 2089 ng/1/2h (± 813) and with alcohol was −69 ng/1/2h ($p < 0.05$) (Figs 5 and 6).

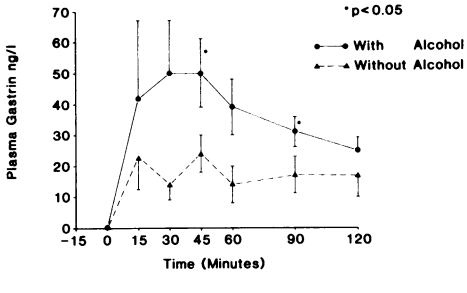


Fig 5. The increase in plasma gastrin concentrations (ng/1) ( ± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

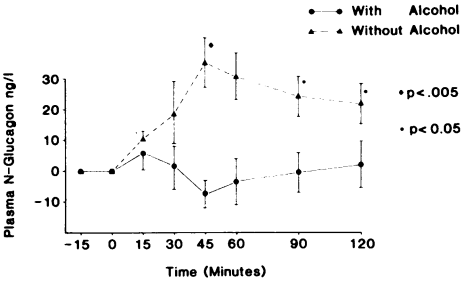


Fig 6. The increase in plasma N-terminal glucagon concentration (ng/1) ( ± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p values refer to the corresponding times comparing with and without alcohol).

There was a tendency towards higher values of C-terminal glucagon without alcohol at all recorded times, but this was not statistically significant. Lower mean levels of pancreatic polypeptide were recorded at all times in the volunteers who had alcohol, but this was only significant at time 90 minutes ($p < 0.05$). The area under the curve with alcohol in two hours was 1560 ng/1/2h, but without alcohol it was 3334 ng/1/2h (Figs 7 and 8).

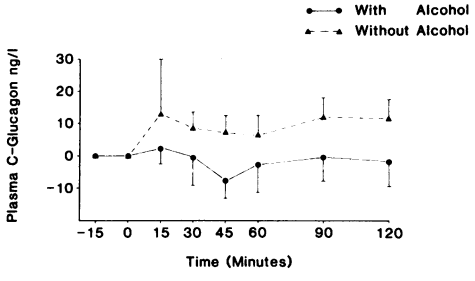


Fig 7. The change in plasma C-terminal glucagon concentration (ng/1) (± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol.

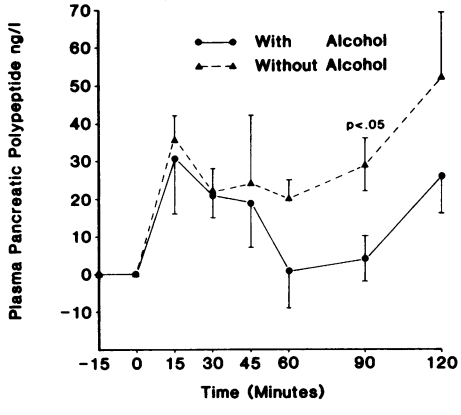


Fig 8. The change in plasma pancreatic polypeptide (PP) concentration (ng/1) (± SEM) in 10 normal volunteers measured over 120 mins following an orange drink containing 34g glucose and 34g fructose, both with and without alcohol. (The p value refers to 90 mins, comparing with and without alcohol).

## DISCUSSION

The experiment was constructed to mimic a common situation, i.e. alcohol taken with a carbohydrate-containing mixer. The total alcohol consumed was approximately equivalent to five U.K. measures (50g) and after dilution with orange juice would be in a concentration of approximately 10% V/V, which is readily absorbable.[10] The peak alcohol concentration (12.4 mmol/l) was at 90 minutes and was still under the limit for legally driving a motor car in Northern Ireland.

Serum glucose was significantly higher in the group with alcohol, as other workers have noted.[11, 12] Alcohol is known to produce vasodilation and this may have promoted the uptake and transport of the glucose. Previous studies with a carbohydrate load given with alcohol have produced hypoglycaemia three to four hours after administration of the test dose.[4] In contrast, our lowest serum glucose recorded was 2.9 mmol/l in one subject at 180 minutes. There was no significant difference in the mean glucose concentrations at 180 and 240 minutes either with or without alcohol and no volunteer complained of hypoglycaemic symptoms. In O'Keefe's study[4] the blood alcohol concentrations were 50% higher than in the present study, and this higher alcohol concentration may have been related to the observed hypoglycaemia in his subjects.

Despite a higher insulin peak with alcohol, there was a similar total release of insulin in both groups and the volunteers with higher serum glucose concentrations did not respond with hyperinsulinaemia. This contrasts with O'Keefe[4] who noted hyperinsulinaemia associated with alcohol administration.

Release of GIP is also glucose-dependent and, while there was a marked response to the orange drink in both groups, there was no overall difference between the volunteers with and without alcohol and this is in keeping with the insulin results. Several authors[2, 9] have noted an increase in serum gastrin after oral alcohol and our results confirm this finding. Stimulation of gastric secretion by oral alcohol is well documented.[13, 14] This may be due to two factors: a direct effect of alcohol on the parietal cells[13, 14] and release of gastrin from the antrum after local action of alcohol.[14] In addition, gastrin release is now known to be stimulated by intravenous alcohol and this seems to be a specific effect of alcohol on the gastrin cells.[15]

As secretin administration has produced all stages of acute pancreatitis in animals[16] and pancreatitis is common in alcoholism, there has been much interest in secretin levels and their relationship to alcohol ingestion. We have found no significant alteration in secretin levels after alcohol; this corresponds with the findings of Henry[3] but is in contrast with the results of Straus[8] and Llanos,[9] both of whom noted secretin stimulation after 60 ml neat vodka taken orally. The previously noted increase in gastrin would be likely to stimulate gastric acid secretion and hence stimulate release of secretin, so it is surprising not to find an overall effect of alcohol on secretin levels. This may be because changes in acid production were not great enough to stimulate any significant release of secretin or because delayed gastric emptying induced by alcohol[17] has reduced the rate of release of acid from the stomach into the duodenum.

The suppression of glucagon by alcohol has not previously been reported. The N-terminal glucagon is more suppressed than the C-terminal glucagon. The C-terminal glucagon antibody reacts predominantly with pancreatic glucagon and the N-terminal glucagon reacts with both pancreatic glucagon and 'entero-glucagon'. Therefore this suggests that alcohol has produced a greater reduction in the 'enteroglucagon' component of glucagon than in the pancreatic component of glucagon. While the physiological functions of 'enteroglucagon' are still unclear, it is thought to be trophic, producing hyperplasia of the small intestinal cells.[18] Since alcohol is known to induce mucosal damage in alcoholics,[19] it is possible that low 'enteroglucagon' levels induced by the alcohol will reduce the gut mucosal response to the alcohol insult. The glucagon findings in the present study are in keeping with those in previous studies of volunteers[3] in which alcohol in the form of 60 ml neat vodka was taken orally and produced no significant change in glucagon when compared with the fasting levels.

The suppression of pancreatic polypeptide (PP) with alcohol is in keeping with previous studies,[6] in which depression of PP levels was noted after a meal with white wine compared with a meal with distilled water. An increase in plasma PP is thought to produce a decrease in exocrine pancreatic secretion[20] and, since alcohol also produces inhibition of exocrine pancreatic secretion in both man[21] and dogs,[22] it has been suggested that PP is the hormonal mediator involved. This hypothesis is refuted by our experiment and by the work of Singer,[6] in which a depression of PP was associated with alcohol ingestion.

In this study, we have found that hyperglycaemia was induced by alcohol but this was not associated with significant overall change in either insulin or GIP levels. While there was stimulation of gastrin release associated with alcohol ingestion, there was no change in secretin release. Pancreatic polypeptide was suppressed in the alcohol group. Suppression of N-terminal glucagon associated with alcohol in this study has not previously been documented.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 191 – 195, October 1985.

# Echovirus type 7 outbreak in Northern Ireland during 1984

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Accepted 26th June 1985.


## SUMMARY

*During 1984, 118 patients with echovirus type 7 infection were diagnosed. The incidence in Northern Ireland was more than three times higher than the rest of the United Kingdom. The outbreak peaked in June and July, with the highest incidence in Belfast and the eastern part of Northern Ireland. All patients were sufficiently unwell to require hospital admission. Aseptic meningitis was the commonest illness (54.2%) followed by gastroenteritis (22.0%), respiratory tract infections (11.9%) and influenza-like illnesses (8.5%). Males (62%) were affected more than females and 50 patients (42%) were less than one year old. The present epidemic had features in common with four previous enterovirus epidemics, except that the under one year age group was predominantly affected and no family or street outbreaks were detected.*


## INTRODUCTION

During 1984 there was an epidemic of echovirus type 7 infection which was unusual because the incidence was higher in Northern Ireland than in the rest of the United Kingdom and children under one year old were mainly affected.

## MATERIALS AND METHODS

Faeces, CSF, throat swabs and acute and convalescent sera were obtained from patients with aseptic meningitis, while faeces, throat swabs or respiratory secretions were obtained from other cases. Primary baboon kidney cell cultures were used for virus isolation. Isolated viruses were typed using echovirus diagnostic serum pools and echovirus type 7 neutralising serum. Acute and convalescent sera from 75 patients from whom echovirus type 7 was not isolated, and who were negative when screened serologically in the microtitre complement fixation test[1] against mumps, measles, herpes simplex and varicella-zoster antigens, were titrated against $100TCD_{50}$ of an echovirus type 7 which had been isolated from the CSF of an aseptic meningitis patient in the current outbreak. The virus/serum mixtures were neutralised for one hour at room temperature before inoculation into Vero cell cultures, which were then observed for cytopathic effect.

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## RESULTS

Echovirus type 7 infection was diagnosed in 118 patients. Sixty-three patients were admitted to Belvoir Park Hospital and 55 to other paediatric and general medical units in Northern Ireland. Virus was isolated from 108 patients. Ten additional patients with aseptic meningitis from whom virus was not isolated had fourfold or greater rising titres of echovirus type 7 neutralising antibody. Echovirus type 7 was isolated from the faeces of 101 patients; from the CSF of 11 patients; from the throat swabs of 6 patients and from respiratory secretions of one patient. The number of patients with echovirus type 7 infection diagnosed in Northern Ireland compared with England and Wales and Scotland in 1984 is shown in Table I.

TABLE I

*Echovirus type 7 infections, 1984*

| | *Number of patients* | *Population (millions)* | *Incidence Cases/100,000* |
|---|---|---|---|
| Northern Ireland | 118 | 1.56 | 7.53 |
| England and Wales[2] | 1009 | 49.60 | 2.03 |
| Scotland[3] | 97 | 5.16 | 1.87 |

The incidence in Northern Ireland was more than three times that of England and Wales and four times that of Scotland. The number of patients and the month of onset of their illness is shown in Table II. The outbreak began in early February, reached a peak in June and July and the last case was detected in mid-November.

TABLE II

*Echovirus type 7 infections, Northern Ireland 1984*

| *Feb* | *Mar* | *Apr* | *May* | *Jun* | *Jul* | *Aug* | *Sep* | *Oct* | *Nov* |
|---|---|---|---|---|---|---|---|---|---|
| 3 | 7 | 9 | 11 | 36 | 38 | 10 | 3 | 0 | 1 |

The illnesses associated with echovirus type 7 infections and the age and sex of the patients are shown in Table III.

TABLE III

*Illnesses associated with echovirus type 7 infections*

| | *Age in years* | | | | | | *Sex* | | *Total* | |
|---|---|---|---|---|---|---|---|---|---|---|
| *ILLNESS* | *<1* | *1-4* | *5-9* | *10-14* | *15-19* | *20+* | *Male* | *Female* | *Number* | *%* |
| Aseptic meningitis | 16 | 4 | 9 | 8 | 5 | 22 | 42 | 22 | 64 | 54.2 |
| Paralysis | — | — | — | 1 | — | — | 1 | — | 1 | 0.9 |
| Gastroenteritis | 19 | 6 | — | — | — | 1 | 15 | 11 | 26 | 22.0 |
| Respiratory | 9 | 4 | — | — | — | 1 | 8 | 6 | 14 | 11.9 |
| Influenza-like | 3 | 1 | 1 | 1 | 1 | 3 | 6 | 4 | 10 | 8.5 |
| Excreter* | 3 | — | — | — | — | — | 1 | 2 | 3 | 2.5 |
| All clinical categories | 50 | 15 | 10 | 10 | 6 | 27 | 73 | 45 | 118 | 100.0 |

* One had clinical and laboratory proven measles, one had varicella and one patient with gastroenteritis had Shigella sonnei in faeces.

It will be seen that more males than females were affected particularly in regard to the nervous system infections. The commonest illness was aseptic meningitis (54.2%). The single case of paralysis was a unilateral lower motor neurone facial palsy in a 14-year-old boy. The second commonest illness was gastroenteritis (22.0%). The respiratory illnesses (11.9%) consisted of upper respiratory tract infection/pharyngitis (seven cases), chest infection (six cases) and chest pain (one case). Echovirus type 7 was isolated from the respiratory secretions of an eight-month-old boy with a chest infection. The influenza-like illnesses (8.5%) consisted of pyrexia, headache and occasionally meningism. Twelve of the 118 patients had erythematous or macular rashes. There were no deaths.

When all age groups were considered, 50 patients (42%) were under one year old and of these 35 were under six months. The youngest, a 10-day-old infant, had pyrexia and a petechial rash, and the oldest patient was a 46-year-old female with chest pains and diarrhoea. The majority of the adult patients (81%) had aseptic meningitis. The patients lived in the following geographical areas:- Belfast (43), Co. Antrim (33), Co. Down (29), Londonderry and Co. Londonderry (9), Co. Armagh (2), and Co. Tyrone (2). There were no recognised family or street outbreaks of echovirus type 7 infection.

A comparison of the main features of the present outbreak with the four previous enterovirus outbreaks is shown in Table IV. It will be seen that the main differences from previous enterovirus epidemics are that the age group most affected was under one year old and that family or street outbreaks were not detected. In the five outbreaks between 1968 and 1984, 574 patients with enterovirus infections were diagnosed.

TABLE IV

*Features of enterovirus epidemics in Northern Ireland 1968-84*

| | | | *Enterovirus* | | |
|---|---|---|---|---|---|
| | *Echovirus 6* | *Coxsackie A9* | *Echovirus 4* | *Echovirus 19* | *Echovirus 7* |
| Year and reference | 1968[4] | 1970[5] | 1970-71[6] | 1974-75[7] | 1984 |
| Number of cases | 95 | 123 | 183 | 55 | 118 |
| Summer peak | + | + | + | + | + |
| Aseptic meningitis—commonest illness | + | + | + | + | + |
| 5-9 year olds mainly affected | + | + | + | + | – |
| Males mainly affected | + | + | + | + | + |
| Most cases in Belfast and in east of N. Ireland | + | + | + | + | + |
| Family outbreaks present | + | + | + | + | – |
| Street outbreaks present | + | – | + | – | – |

(+ feature present; – feature absent).

## DISCUSSION

This is the fifth major enterovirus epidemic to occur in Northern Ireland in the last 17 years and is the first known echovirus type 7 outbreak. Echovirus type 7 was last isolated from six patients in 1980 and from one patient in 1981. An echovirus type 7 outbreak occurred in the north of England in 1980 and this may partly explain the more than threefold lower incidence in the rest of the United Kingdom compared with Northern Ireland in 1984. While the peak of the Northern Ireland

outbreak was in June and July, the data from England and Wales showed a summer peak in some areas but overall most cases occurred in the fourth quarter of the year. The Scottish outbreak also showed a peak in the fourth quarter of the year.

Our results show that echovirus type 7 was present more often in faeces than in throat swabs or respiratory secretions and this may indicate that spread is more likely to be by the faecal-oral rather than by the respiratory route.

As in previous outbreaks, the commonest illness was aseptic meningitis (54.2%) which predominantly affected males. Gastroenteritis (22.0%) was followed by respiratory infections (11.9%) and influenza-like symptoms (8.5%). The commonest illness in the under-one-year-olds was gastroenteritis and in adults it was aseptic meningitis. It must be remembered, however, that only patients admitted to hospital were investigated virologically. In other enterovirus infections such as poliomyelitis in young children it is known that the ratio of subclinical to clinical infections may be as high as 1000 to 1.[8] Undoubtedly many minor unreported illnesses and subclinical infections associated with echovirus type 7 infection have occurred in the community, and these would not have been investigated.

The age group involved in this outbreak is of considerable interest since it differs from that of the four previous enterovirus epidemics. In the latter epidemics the 5-9 year old age group had been most affected and this correlates with the increased infection rate associated with starting school. The infection of 50 children under one year old and in particular the 35 children less than six months old raises interesting questions as to how they became infected. These children would not be mobile and would have close contact only with parents and other siblings. Spread was almost certainly faecal/oral but family or street outbreaks of infection were, surprisingly, not found, unlike previous outbreaks of enterovirus infection. Despite the absence of recognised family infections, subclinical infection in other members of the families seems the only way that infection could have been transmitted to affected infants. Contamination of water, milk or food with echovirus type 7 is a possibility, but there is no evidence for this assumption. It is also possible that a large section of the population is immune from previous echovirus type 7 infections which had been unrecognised, and that only the very young are now susceptible. However, 27 patients (22.8%) in this study were adults, which suggests that they too were susceptible. The geographical areas where the patients lived were similar to previous enterovirus outbreaks, i.e. Belfast and the eastern part of Northern Ireland and this correlates with the distribution of population.

The first four enterovirus epidemics have shown a remarkably constant pattern in the main features. The present echovirus type 7 epidemic has shown two differences, namely the predominance of cases in the under-one-year-olds and in the absence of recognised family or street outbreaks.

We thank the Communicable Disease Surveillance Centre, Public Health Laboratory Service, London, for data relating to England and Wales, and the Communicable Diseases (Scotland) Unit, Glasgow, for data relating to Scotland.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 196 – 199, October 1985.

# PUVA therapy for psoriasis: choosing a suitable régime

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Accepted 6th June 1985.

## SUMMARY

*Three age- and sex-matched groups of 30 patients with chronic plaque psoriasis were treated by photochemotherapy (PUVA). Groups I and II received routine maintenance PUVA therapy at different intervals and Group III had no maintenance treatment. The remission time after the clearance treatment with PUVA is compared with the total cumulative dose of long wave ultraviolet light (UVA). A lower mean dose of UVA (51.0 ± 1.7 joules/cm²) in Group III (no maintenance PUVA) achieved a comparable remission period to that after larger cumulative doses following routine maintenance therapy (87.8 ± 4.9 and 77.0 ± 4.1 joules/cm² in Groups I and II).*

## INTRODUCTION

Photochemotherapy using long wave high intensity ultraviolet rays and oral psoralen (PUVA) is an effective although palliative treatment in chronic psoriasis[1] with therapeutic efficacy comparable to dithranol application.[2] Patient acceptance is high owing to minimal use of ointments, but potential long-term hazards have not been clearly delineated. It is widely recognised that the possibility of premature ageing, skin cancers, cataract formation, pigmentary changes and alteration in the immune system are potential risks associated with PUVA therapy.[3] It is often necessary to use therapy continuously with consequent high total cumulative doses of long wave ultraviolet rays (UVA). The problem of finding safe and effective treatment for chronic plaque psoriasis remains, and dermatologists are constantly striving to find an effective but safe protocol for administering PUVA therapy. There is no general agreement as to whether a maintenance regimen should be used or, if a maintenance regimen is used, what form is effective with minimum exposure to UVA. Since PUVA therapy became available in our skin unit we have been revising our treatment protocol in the light of available data on PUVA therapy. There are only a few published reports concerning the remission period following PUVA therapy and its relationship to total UVA exposure. By constantly revising the treatment protocol, it became possible to compare various régimes of PUVA therapy administered to our

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patients with psoriasis. The object of this retrospective study is to compare groups of patients who had maintenance PUVA with a group who had received no maintenance therapy with PUVA and to relate the total UVA exposure to the length of remission period.

## PATIENTS

Only patients with chronic stable plaque psoriasis were selected for the study. All patients were assessed according to already published criteria[2] prior to starting PUVA therapy. Full clinical examination and laboratory tests (haemoglobin, total white cell count, platelet count, serum bilirubin, alkaline phosphatase, aspartate and alanine transaminase, gamma gluteryl transpeptidase and blood urea) were carried out to exclude co-existing medical problems. The laboratory tests were repeated once during the treatment and at the completion of PUVA therapy in each case. A detailed ophthalmological examination was performed before starting PUVA therapy and after the therapy in all cases. Only those with type II skin were included in the study. All had extensive involvement of their skin with psoriasis, more than 10% of their body surface. Age ranged from 18 to 70 years, mean 37 years. Three groups of 30 patients matched for age and sex were analysed, depending upon the maintenance regimen of PUVA therapy used.

## PUVA THERAPY

All patients were treated with PUVA three times weekly until their psoriasis resolved completely, and thereafter according to the maintenance regimen described below. The drug 8-methoxypsoralen was used in a dosage of 0.6 mg/kg body weight, given two hours before the UVA exposure. The initial dose of UVA was 1.5 joules/cm$^2$, increasing by 0.5 to 1.00 joules/cm$^2$ every 3 – 4 treatments according to individual needs, using a Waldman 'PUVA 4000' unit.

Clinical clearance was considered to have occurred when the psoriatic lesions had flattened completely, both visually and on palpation. The time taken to clear the psoriasis ranged from 4 to 10 weeks.

*Group I.* After clearance of psoriasis this group was given weekly maintenance treatment with progressive lengthening of the interval between treatments finishing with one treatment every 3 – 4 weeks. This period of maintenance PUVA was approximately 4 months. At this stage PUVA therapy was stopped.

*Group II.* After the clearing regimen, patients were treated once every 3 weeks with maintenance PUVA. Duration of maintenance varied from 6 to 7 months.

*Group III.* After the clearing regimen, no maintenance treatment was given.

All patients were reviewed at 2 months after stopping PUVA therapy and thereafter if they relapsed. A relapse was considered to have occurred with the development of new lesions of psoriasis involving about 5% of the body surface. Remission time was calculated from the time clearance therapy was stopped until relapse. Patients were observed for a period ranging from 2 months to 24 months. Statistical analysis was performed using the paired t test.[4]

## RESULTS

The number of treatments to clear psoriasis in each group was the same (Table). The three groups had similar durations of remission. No difference was observed between groups either in the mean total number of treatments needed to clear

psoriasis or in the length of remission achieved. Group III received a lower dose of UVA to achieve the same duration of remission than Groups I and II ($p < 0.0005$), and Group II received less than Group I ($p < 0.05$).

TABLE

*Average number of clearing treatments, mean dose of UVA and mean duration of remission in 3 groups of patients with psoriasis on PUVA therapy*

| Group | Average number of treatments on clearing regimen (± SEM) | Dose of UVA joules/cm² (± SEM) | Duration of remission (months ± SEM) |
|---|---|---|---|
| I | 21.0 ± 0.8 | 87.8 ± 4.9 | 8.53 ± 0.6 |
| II | 21.2 ± 0.6 | 77.0 ± 4.1 | 9.20 ± 0.5 |
| III | 21.6 ± 0.5 | 51.0 ± 1.7 | 8.77 ± 0.6 |

Nausea and itching of the skin were the only reported side effects. Mild nausea was common, but in only five patients was it severe. Eight patients had mild to moderate itching during PUVA therapy. No other serious side effects were observed in the patients studied. No haematological or biochemical changes were detected. No ophthalmological changes were found in any of the patients studied.

## DISCUSSION

We studied three groups of 30 age- and sex-matched patients with chronic plaque psoriasis who had received PUVA therapy, and found that it is possible to obtain a reasonable period of remission from psoriasis with or without maintenance PUVA therapy. There are relatively few reports about the lengths of remission periods after stopping PUVA therapy.[5, 6, 7, 8, 9] In these reports the remission period after clearing treatment varied from 5 weeks to 8 months, and our results are in agreement. The value of maintenance therapy with PUVA was first questioned in 1977 when PUVA therapy had just been introduced.[10] Other workers[7, 8] claim that maintenance treatment will prolong the remission periods and thus reduce the total cumulative UVA dosage received by the patients even if they have to go back on a clearing regimen at a later date. Our results do not support this view in that the remission period was similar in all the groups studied whether or not maintenance PUVA was used. However, Warin in a later study[11] reported that recurrent courses of PUVA therapy may reduce total cumulative UVA exposure and economic cost. We would agree with this observation and can keep the cumulative UVA dosage significantly reduced with no maintenance PUVA, while still achieving a comparable remission period. Owing to the markedly reduced dose of UVA received by patients who had no maintenance PUVA, we consider that after the clearing regimen PUVA therapy should be stopped and clearing courses should only be repeated if required owing to relapse.

The risks associated with PUVA therapy will almost certainly be due to the cumulative total UVA exposure. The cumulative effects of continued treatment are not yet known. Various modifications such as low-dose PUVA,[9] frequent rest periods between treatments and combination with other agents such as retinoids[12] may be instituted to reduce the cumulative UVA dose.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 200 – 203, October 1985.*

# Thompson House Centenary, 1885 – 1985

J H D Millar

Address given at the Centenary Celebrations of Thompson House.

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The 'Thompson Memorial Home for Incurables', now Thompson House, was completed and ready for the admission of patients in February 1885. This very fine building in the Queen Anne style stands on the Magheralave Road, Lisburn, nearly opposite the Friends' School. It is a memorial to William Thompson Esq, MD, FRCSI, born 7th March, 1806. He had been surgeon to the County Antrim Infirmary, Seymour Street, Lisburn, for many years and was killed in an accident on the level crossings at Dunmurry on the 22nd September, 1882. His house stood where the Fire Authority is now situated and his memorial and grave are in the graveyard of Lisburn Cathedral. By law he had been compelled to discharge from the Infirmary all patients considered incurable. He had frequently expressed the pain it gave him to comply with this enactment, and deplored the absence of some asylum to which such persons might be sent.

His widow Rosina Thompson, his daughter Mary Hogg Bruce and son-in-law James Bruce, JP, Deputy Lieutenant for the County of Tyrone, agreed to allocate the sum of £60,000 (about £1 million by present day value) of the assets from the estate of Dr Thompson to build and endow a home for incurables. On the 5th May, 1883, the above founders bought a nine acre site for the Home from Sir Richard Wallace for £901 in the townland of Lisnagarvey, Blaris Manor of Killultagh, Barony of Upper Massereene. Sir Richard Wallace, of Wallace Collection fame, was MP for County Antrim from 1873 to 1884 and had made many generous gifts to Lisburn, but none compared with the munificence of the Thompson bequest. Sir Richard leased and lived in Antrim Castle and travelled by private train to and from Lisburn. It is very likely that the Thompson family attended parties given at Antrim Castle by Sir Richard. The architect of the new building was Mr G Ferguson and the contractor Mr Robert Corry, both of Lisburn. Mrs Thompson was able to visit the work in progress before her death on the 8th December, 1884. Her daughter Mrs Bruce gave a further £10,000 in memory of her mother. The Bruce family maintained a very close personal interest in the management of the Home and the welfare of the residents. Mr M R Bruce of Corriewood, Castlewellan was president of the Board of Management when the Home was finally taken over by Antrim County Council in 1963.

The first Trustees were John Blakiston Houston, JP, DL, Henry Shaw Ferguson, MD, Canon William Dawson Pounden, Ogilby Blair Graham, JP, James Theodore Richardson, JP, and Henry Jones McCance, JP. They were responsible for the land and building, also endowments of £38,000 and any further money and its proper investment. A General Committee was formed consisting of 27 well-known persons from the Lisburn and Belfast areas. No ladies were to serve on the General Committee apart from the surviving founder, Mrs Mary Hogg Bruce. A Board of Management was appointed by the General Committee to

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J H D Millar, MD, FRCP, Honorary Consultant Neurologist.


THOMPSON HOUSE

supervise day-to-day management and at least five ladies were to serve on the Board of Management. Dr George St George was appointed medical officer and Dr Samuel Musgrave and Dr H S Ferguson accepted the office of honorary physicians to the Home.

It is not clear how many patients were originally admitted but when the Home was taken over by the Antrim Health Committee in 1963 there were 60 residents. The Home was to be 'devoted to the care of the respectable poor suffering from incurable disease and shall not be available for persons whom the Board of Management might think ought to be treated in the workhouse hospitals, nor for those who are in comfortable circumstances, nor for idiots, or persons of unsound mind, nor for persons under sixteen years of age. Applicants having small means of their own, but not enough to support them comfortably, shall be eligible for admission to the Home; the Board of Management may stipulate that they contribute to their support'. Under certain circumstances full paying patients could also be admitted.

One of the bye-laws stated that 'patients should have been a resident for five years in one or more of the Counties Antrim, Armagh, Londonderry, Down, Monaghan or Tyrone. The Board must also be satisfied that no applicant is a person of bad character'. The religion of the applicant was in no way to be taken into account and the Institution was to be strictly non-sectarian.

About 1960 when Major Charles Blakiston Houston was chairman, the endowments could no longer cover the cost of upkeep and it was decided to make a small charge to the residents. Approaches had been made to the Northern Ireland Hospitals Authority without success but in January, 1963, the Antrim County Council took over the responsibility of the Home with endowments of £80,000.

Considerable renovations and improvements were carried out by the County Council costing, together with furniture and equipment, some £170,000. Work was completed in 1967 and the Home, thereafter called Thompson House, was formally opened by the Governor, Lord Erskine of Rerrick, on 9th October, 1967.

The County Medical Officer, Dr W Bamber, made it clear that the traditions of the Home should be continued and that persons admitted to Thompson House should be chronically handicapped patients in the younger age groups. A small sum was set aside to honour the founder's wish concerning the eligibility of residents of County Monaghan.

I am much indebted to Dr J S Y Mathewson for the following:

> 'I joined the late Dr J G Johnston, MC, as an assistant in 1954. He had, I believe, been Medical Officer to Thompson Home for many years prior to that date. I well remember my first visit there with him. The notice at the entrance gates read "Thompson Memorial Home for the Incurables" — not a hopeful sign for the residents! I was introduced to the Matron, Miss Duffield and the two nursing sisters, Miss Kelly and Miss Taylor. We all accompanied Dr Johnston on his ward round. The residents were mainly elderly and quite a number were bedridden. The wards were scrubbed wooden floors and there was an open fire in each of them. This gave a cheerfulness and homeliness to the wards, but of course caused a good deal of work in carrying the coal upstairs and in dusting the wards. Dr Johnston was a life-long admirer of the works of Gilbert and Sullivan and I remember him rendering a chorus from *The Mikado* in one of the wards on that visit. The residents were well cared for, but of course the standards did not compare with those of to-day. Patients were treated there until they died and I do not recall anyone being transferred to another hospital for further treatment. Some of the residents I remember well, in particular Miss Maggie Moore, Miss Florence Walker and Mrs Mary Bell. I am delighted to say that Mrs Mary Bell who was a resident before I came in 1954 is still a resident with us today.
>
> 'I remember that each Christmas morning the Lisburn Silver Band came to play on the driveway outside the Home as they still do. Dr Johnston and I attended and helped to carve the turkeys and hams. We also helped to serve the residents.
>
> 'The number of residents gradually diminished over the succeeding years and in 1963 the County Antrim Health Committee was asked if they would be interested in taking over the running of the Home. There were numerous meetings with Mr Robinson, Chairman, Mr Penington, Secretary, Dr Bamber, Medical Officer, and Miss Massey, Nursing Officer, and finally they agreed to take it over and to rename it Thompson House. The future residents were to be under 55 years of age and to be physically handicapped. This having been decided, the building was closed for renovations. All residents were dispersed to other residential homes and geriatric wards with the promise that they would be taken back into residence when the alterations were complete. The promise was kept. Miss Russell was appointed Matron and when she resigned in 1972 Mrs E King, our present Nursing Officer in Charge, was appointed her successor. Thompson House soon became filled with the young handicapped. Many of them were suffering from multiple sclerosis and the local Multiple Sclerosis Society soon began to take an active interest in the residents'.

On April 1st 1975 Thompson House was taken over by the Eastern Health and Social Services Board and designated a hospital. In 1976 Dr Taggart, Chief Administrative Medical Officer, Eastern Health and Social Services Board, asked me if I would act as visiting consultant which I was pleased to do until my retirement in 1982, when I was succeeded by Dr Michael Swallow.

Thompson House Hospital now has 53 beds which are constantly occupied. Over the last few years there has been a move towards introducing more beds for holiday relief and some beds for medium term rehabilitation. The two purpose-built chalets in the grounds provide excellent training in aspects of daily living for patients who are expecting to be discharged home. About 40% of the residents suffer from multiple sclerosis, some 15% from the effects of trauma and another 15% from strokes. Other conditions include cerebral palsy and rheumatoid arthritis. About two-thirds of the patients are under the age of sixty and patients are not generally transferred when they come into the geriatric age range.

There is a well-trained nursing staff under the Nursing Officer, Mrs E King, and Sisters E Walsh and R M McStay. In addition there are two part-time physio-therapists and an occupational therapist. The social worker and speech therapist visit as necessary. The voluntary organisations make substantial contributions to the comfort and welfare of patients, helping with visiting and outings. These include the Multiple Sclerosis Society, the Chest, Heart and Stroke Association, the British Red Cross and the Lions' Club. The 'Friends of Thompson House' have recently been formed and help with outings, picnics, and barbecues and contact with local organisations for the disabled. The hospital has a small bus and most patients go on holidays in the summer, often accompanied by members of staff and even their families. Art therapy sessions were introduced in 1984 and have proved very popular. Musical entertainment is provided by many local groups, choirs, bands and visiting professionals. Dr Swallow sometimes plays the piano for the residents on his weekly visits.

Thompson House can be proud of its past and present achievements and will continue to strive to create a stimulating and caring environment for younger people with severe physical handicap.

I wish to thank Dr P M Darragh, Eastern Health and Social Services Board, for his help in finding the legal documents regarding Thompson House.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 204 – 207, October 1985.

*Case report*

# Awake blind nasal intubation

K R Milligan, N T Kenny

Accepted 1st October 1985.

Awake blind nasal endotracheal intubation is a modification of Sir Ivan Magill's technique of blind nasal intubation under ether anaesthesia.[1] The introduction of neuromuscular blocking agents, facilitating oral intubation under direct vision, led to a decline in popularity of Magill's method and it is now used sparingly, if at all.[2] Where the sedated patient remains awake and co-operative, the technique still deserves greater attention.[3] The indications vary from the elective to the mandatory and include:

Deformities of the mouth or temporomandibular joints (rheumatoid arthritis, ankylosing spondylitis[4]), Ludwigs angina or any potential cause of upper airway obstruction.

Gastrointestinal obstruction or bleeding.

Unfasted patients or cases in which rapid intubation techniques may be hazardous (perforating eye injuries, poor risk patients).

Dental problems such as extensive reconstruction.

Three cases are described which illustrate the contribution that this technique can make to a patient's anaesthetic management.

*Case 1*

A 47-year-old woman was admitted with a second recurrence of a right paratid carcinoma. The two previous anaesthetics, with oral intubation, were uneventful, the more recent having been 10 months previously. On pre-operative examination she was found to have a right lower motor VIIth nerve palsy, a firm swelling over the temporomandibular joint and a receding chin. Mouth opening was limited to approximately 3 cm because of pain from the joint area. There were no other significant findings and she was premedicated with 10mg of oral diazepam. After preoxygenation in theatre, sodium thiopentone 300mg was administered followed by suxamethonium 70mg. Because of trismus of the jaw, relaxation was not sufficient to permit oral intubation. A good airway could be maintained and the patient was allowed to waken up. Blind nasal intubation was decided upon and the situation explained to the patient who was then sedated with ketamine 10mg and diazepam emulsion (Diazemuls) 5mg. She was positioned with a 45° head uptilt and the left nares was carefully swabbed with viscous lignocaine 4% plain, several minutes being allowed for it to take effect. The oropharynx was then sprayed carefully and slowly from above downwards with 4% lignocaine plain, care being taken not to exceed the toxic dose

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(3mg/kg). A further 1.5ml of 2% lignocaine plain was injected rapidly through the crico-thyroid membrane at the end of maximum expiration, the cough following inspiration spreading the solution over the sublaryngeal area. A size 7.0 cuffed Portex endotracheal tube, softened in warm water, and lubricated with lignocaine jelly was then slowly and gently passed through the left nares, and using breath sounds as a guide[3] the trachea was entered easily. Anaesthesia was then induced with thiopentone 200mg and the operation proceeded uneventfully.

*Case 2*

A 64-year-old man presented for an excision biopsy of a large right submandibular swelling (Fig 1), later shown to be a salivary gland adenocarcinoma. He had previously been rejected as unfit for surgery due to chronic obstructive airways disease, obesity and continued heavy smoking. He could walk only 50 metres and previous admissions included an episode of respiratory failure requiring ventilatory support. The lesion had recently begun to enlarge rapidly, forcing intervention. He was premedicated with temazepam 20mg orally. In theatre both nasopharynx and oropharynx were carefully sprayed with 4% lignocaine, but the larynx could not be visualised. Droperidol 5mg, diazepam emulsion 5mg and ketamine 10mg were given intravenously and the nares swabbed with the viscous lignocaine. An injection of 2ml 2% lignocaine plain was given rapidly through the crico-thyroid membrane. Some difficulty was encountered due to nasal obstruction but after several attempts a softened cuffed 6.5 Portex tube was passed and the trachea entered. Anaesthesia was induced uneventfully and following elective overnight ventilation the patient was weaned from the ventilator and extubated without difficulty.

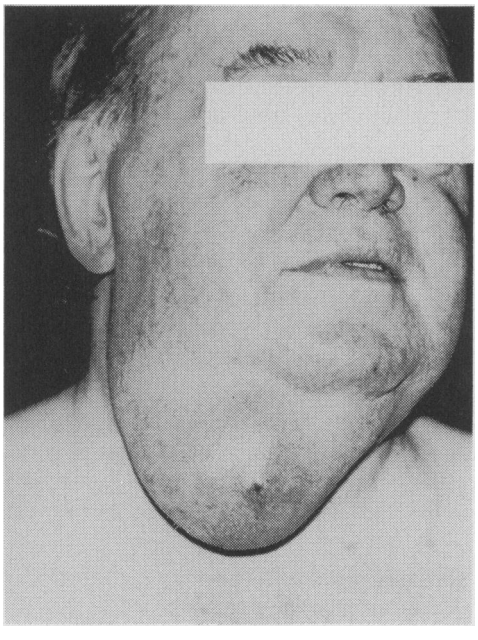

Fig 1.
Case 2—Salivary gland adenocarcinoma.

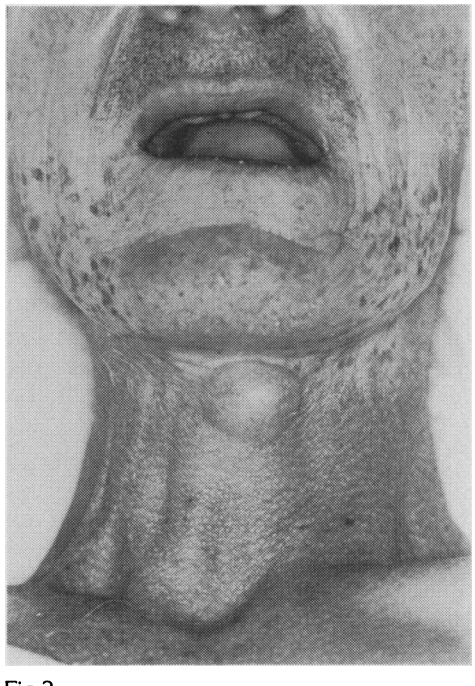

Fig 2.
Limited mouth opening and neck extension.

*Case 3*

A 54-year-old man was admitted with signs of a large bowel obstruction. He was vomiting and dehydrated and had marked abdominal distension. Four years previously he had undergone fast neutron radiotherapy for a squamous carcinoma of the tongue. This had resulted in marked fibrosis of the cervical and mandibular regions allowing only limited neck extension and mouth opening (Fig 2). Following initial resuscitation and the same preparation and medication as Case 2, a softened 7.5 endotracheal tube lubricated with lignocaine jelly was passed through the left nostril and the trachea entered. Anaesthesia was induced uneventfully and a colonic carcinoma resected. Despite pre-operative suction of the patient's naso-gastric tube, a total of 900ml of fluid was aspirated intra-operatively out of the stomach underlining the danger of aspiration into the bronchial tree.

## COMMENT

All these patients were drowsy but co-operative, responding readily to commands. In no case was the airway in danger at any time. Important points in this technique are:

*Position:* The table is broken with a 45° head uptilt. This allows easy manipulation of the head and neck and is comfortable for the patient although the anaesthetist may have to stand on a platform. The tilt may also help prevent regurgitation of stomach contents.

*Adequate sedation:* The patient must be calm and tolerant. The combination of drugs was designed to calm the patient while retaining co-operation for deep breathing. Droperidol is a sedative widely used in neuroleptic techniques while diazepam has useful sedative and amnesic actions and ketamine is a potent analgesic.

Despite good sedation, the procedure will be unpleasant if topical analgesia is inadequate. The application of this must be painstaking and, in particular, time must be allowed for it to take effect. This technique is not suitable if rapid intubation is required. Cocaine as a 10% solution may also be used for topical anaesthesia[5] and has the advantage of producing shrinkage of the nasal mucosa. Crico-thyroid puncture with the injection of 1 – 2ml of lignocaine plain is a useful adjunct provided that the neck can be extended sufficiently. It provides sublaryngeal anaesthesia and diminishes the explosive coughing which can accompany the entrance of the endotracheal tube into the trachea.

*Patient acceptance:* The patients were interviewed post-operatively and none had found the experience particularly unpleasant. This is important since repeat anaesthesia may be necessary. All three cases required further surgery.

Fears have been expressed concerning the danger of aspiration due to depression of protective laryngeal reflexes. It is our experience that the patients cough as the tube enters the larynx, indicating that the reflexes, although modified, are not completely obtunded and we have not experienced any problems in this respect. Fibreoptic laryngoscopy may be used as a refinement of this technique but requires equipment and training.[6]

Awake blind nasal intubation offers a safe, simple and effective method of intubation in difficult cases.

We wish to thank Dr J Moore for his help and advice and Mr T K Day and Mr M Bell for permission to report these cases.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 208 – 210, October 1985.*

*Case report*

# Reversible Holmes' syndrome complicating cardio-pulmonary resuscitation

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Accepted 24th July 1985.

The two cardinal features of the syndrome described by Holmes in 1918[1,2] are a disorder of ocular movement and a disorder of spatial orientation. The former is manifested by severe problems of ocular fixation and accommodation, such that the patient finds great difficulty in fixing his or her gaze on an object and, having done so, has even greater difficulty in moving the point of fixation to look at something else. This means, for instance, that he cannot follow a moving object with his eyes. The second feature means that the patient has difficulty in orientating objects in three-dimensional space, so that he cannot pour a glass of water without spilling it, and, as in this case, has difficulty in lifting food with a fork or spoon. It can also result in disturbance of topographical memory so that he cannot find his way around, even in familiar surroundings. Other features found in some, but not all of Holmes's original six cases include: hemiparesis, hemisensory loss, speech disorders, visual field defects, visual neglect and apraxia.

## CASE HISTORY

A 57-year-old right-handed housewife was admitted to the coronary care unit following an acute inferior myocardial infarction. Three hours after admission she had the first of a series of four episodes of ventricular fibrillation. During the last of these, she required a period of cardio-pulmonary resuscitation lasting 45 minutes and artificial ventilation for a further 48 hours. It was another four days before a normal level of consciousness was restored. She then complained of being unable to eat because she 'kept missing her food with her fork' and of being unable to read.

On examination of the central nervous system there was no weakness, sensory loss, hemianopia, or unilateral neglect. Comprehension of speech and cognition were unimpaired, but she had a nominal dysphasia. When she wore her normal glasses, visual acuity was bilaterally 6/6 though she said that it took several seconds for objects to come into focus. She was able to move her eyes in any direction on command, though if the eyes were fixed on a particular object and a

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torch was flashed in her peripheral visual field, the normal saccadic searching eye movements in the direction of the new stimulus were absent. On being asked to read, she could normally make out a single word but scanning movements were absent.

There was great difficulty in orientating objects in three-dimensional space, so that she missed when asked to grasp an object held out by the examiner, and could not pour a glass of water, or pick up a piece of food with her fork. There was a disorder of topographical memory so that she frequently had to stop and ask for directions on her way to the toilet, which she could clearly see and recognise from her bed. In addition, she demonstrated all the signs of a Gerstmann syndrome (right/left disorientation, finger agnosia, acalculia, agraphia). She had good insight into all her disabilities.

At the time of discharge, four weeks after the cardiac arrests, her dysphasia had resolved, but her other signs were unchanged so that she had difficulty finding her way around her own home. Unfortunately, she refused to attend follow-up or for CT scan, and was not seen for a further two months. She then consented to attend an outpatient clinic, but not to undergo further investigations. Neurological examination at this time was entirely normal and her disorder of topographical memory had resolved to the extent that she could go out to the local shops. She has remained well at subsequent review.

## DISCUSSION

Holmes' syndrome is best considered as a development of that described by Balint in 1909,[3] though an earlier description exists.[4, 5] Balint did not note the specific problem of ocular movement which is a major feature of Holmes' syndrome but referred to 'optic ataxia' in his patients. It is probable, however, that both Holmes and Balint were describing the same clinical picture, and the terms are therefore interchangeable, though some authors have argued otherwise.[6]

Reports have been published of sporadic single cases and short series of patients with the disorder, including a case initially presented in this journal.[6, 7, 8, 9, 10] Although few cases have come to post mortem,[4, 9, 10] or had the benefit of newer radiological techniques, it is agreed that the causative lesion is bilateral posterior parietal lobe damage, as in Holmes's six victims of penetrating head injury.

The occurrence of 'minor forms'[9, 11, 12] of the syndrome have led to the suggestion in this case, as in the case of Gerstmann's syndrome,[13] that the clinical findings represent a constellation of separate neurophysiological deficits, related only because it is possible for them to be caused by a single vascular or traumatic event. Certainly, the disorder of ocular fixation is similar to that found in the affected visual field of a stroke patient with marked unilateral visuo-spatial neglect. In two of Holmes's patients[1] and one of Hécaen's,[9] the ocular disorder was more marked in one visual field. A lateralised disorder of topographical memory also occurs in visuo-spatial neglect,[14, 15] and a non-lateralised form in bilateral stroke.[16, 17] It is interesting to speculate, therefore, whether some of the features of Holmes' syndrome could be explained on the basis of bilateral visuo-spatial neglect. Despite the possibility that Holmes' syndrome is not a distinct entity, it is important, as in the case of Gerstmann's syndrome, that the various features should be recognised in the clinical setting. Because they are unusual, it is possible that they could go unrecognised, or be misinterpreted as evidence of mental confusion.

The clinical findings in this patient accord well with Holmes's original cases,[1] and all the features of the syndrome were present. There are two notable points to be drawn from this case report. First, Holmes' syndrome developed following cardiac arrest. There have been previous reports of Holmes' syndrome complicating occlusion of both internal carotid arteries[6] and cardiac surgery,[18] the posterior parietal 'watershed' areas being particularly susceptible to anoxia. Holmes' syndrome is a potentially disabling complication of cardiac arrest which may not be recognised because of its unusual clinical features, and may be commoner than previously supposed. Second, the syndrome resolved completely over a three-month period. Previous studies have tended to suggest that, once it has developed, Holmes' (or Balint's) syndrome is a permanently disabling condition.[7,8] As in other forms of cerebrovascular damage, the exact mechanisms of recovery are unclear. It may be postulated that recovery of local oedema and the revitalisation of a 'penumbral' area of cerebral tissue which had not been irretrievably damaged were involved. In the past, this disorder was often diagnosed some time after the cerebral damage had occurred, when the period of maximum spontaneous recovery had already passed, and it is feasible that the condition remained undiagnosed in those in whom recovery had occurred.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 211 – 213, October 1985.

*Case report*

# Infarction of a caecal lipoma simulating appendicitis

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Accepted 4th July 1985.

Lipomas of the large bowel are rare, and their infarction has seldom been reported. In the present case, the symptoms and signs were suggestive of appendicitis and the final diagnosis of the infarcted caecal lipoma was made only after right hemicolectomy had been performed and the specimen had been examined histologically. Further investigations uncovered paroxysmal nocturnal haemoglobinuria, a form of haemolytic anaemia, which may have contributed to infarction of the tumour.

## CASE HISTORY

A 64-year-old man was admitted with a four-day history of generalised abdominal pain, settling on the right side. He was anorexic and nauseated. One loose stool had been passed 24 hours prior to admission. He had a mild pyrexia and was slightly jaundiced. There was tenderness with rigidity and rebound in the right iliac fossa, but the bowel sounds were normal. A diagnosis of appendicitis was made, with carcinoma of caecum as the differential diagnosis.

Laboratory investigations: haemoglobin 10.4 g/dl, white cell count $7.9 \times 10^9/l$, mean corpuscular volume 105 fl (79-97), total serum bilirubin 70 umol/l, serum alkaline phosphatase 665 iu/l (115-320), serum gamma-glutamyl transpeptidase 179 iu/l (10-45), and serum amylase 125 iu/l (70-300). Abdominal radiographs gave no evidence of intestinal obstruction or perforation.

At operation the appendix was normal but a tumour was palpable in the posterior wall of the caecum. The adjacent colonic muscle was oedematous and the greater omentum was adherent to it. There was excessive fatty tissue in the bowel mesentery and in the right paracolic gutter. Right hemicolectomy was performed. Pathological examination of the hemicolectomy specimen revealed a 4.5 cm long soft, red, polypoid tumour situated in the caecum, 4 cm from the ileo-caecal valve. The colon for 5 cm distal to the tumour was thickened and oedematous.

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Histological examination revealed a submucosal lipoma which had undergone haemorrhagic infarction (Figure). The ghost outline of overlying mucosal glands was seen. The submucosa was thickened and contained numerous necrotic fat cells with blood debris and inflammatory cells. The muscle coat was necrotic; fibrin thrombi were present in vascular channels within the tumour and at the serosa. The adjacent colon contained an excess of submucosal fat and the appendix showed fibro-fatty obliteration.

Figure. Haemorrhagic infarction of submucosal lipoma. Attenuated mucosa at top of photograph, and degenerating muscle coat at bottom. (H and E × 20).

Post-operatively, the patient's jaundice deepened until the fourth day (total bilirubin 151 μmol/l, alkaline phosphatase 347 iu/l) and then regressed. Further investigation showed that he suffered from paroxysmal nocturnal haemoglobinuria, a form of acquired haemolytic anaemia. The abdominal condition settled, and he was discharged from hospital on the 10th post-operative day. He has been followed up for two years and remains free from abdominal pain and rectal bleeding. To compensate for haemolysis he requires supplements of iron, folic acid and hydroxocobalamin, with occasional transfusion of washed red cells.

## DISCUSSION

Intestinal lipomas are rare. Their usual site is the submucosa of the large intestine[1] and they are more frequent on the right side of the colon than on the left.[2] Only a minority cause symptoms, and these lipomas are likely to exceed 2 cm in diameter.[3] Two lipomas have been found as synchronous tumours in the colon,[4] and rarely there is diffuse lipomatosis of the wall of the large intestine involving the submucosa and subserosa and extending widely into the adjacent part of the mesocolon.[5, 6] The condition known as fatty infiltration or lipomatosis of the ileocaecal valve simulates a tumour in the caecum but is not considered to be a true neoplasm.[7]

The various symptoms and signs produced by these tumours[4] may be attributed to intussusception, infarction or occult faecal blood loss. Only one case of infarction has been reported[3] in three series, comprising 53 symptomatic cases.[2, 3, 4]

When the diagnosis of lipoma is made pre-operatively by barium enema or colonoscopy, local excision of the tumour or segmental colonic resection is performed, but in an emergency wide resection is often necessary, because the tumour is considered to be malignant. The coexistence of lipoma with carcinoma or adenoma is well established,[2] and usually carcinoma is the symptomatic

tumour. However, in 38 cases of symptomatic lipoma, adenomas of the large bowel were found incidentally in 12 (32%).[4]

Paroxysmal nocturnal haemoglobinuria is associated with mesenteric and hepatic vein thrombosis. It is possible therefore that the blood disease contributed to infarction of the tumour. The large mesenteric veins were not thrombosed, however, and the patient has had no further episodes of thrombosis while under review for two years. The oedema and haemorrhagic necrosis of the muscle in the ascending colon suggest that intussusception had commenced but was prevented by peritoneal tethering of the colon.

We wish to thank Dr Philip Burnside, Consultant Haematologist, for his assistance in the diagnosis and management of the patient's haemolytic anaemia, and Mrs Ethna Law, who typed the manuscript.

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The Ulster Medical Journal, Volume 54, No. 2, pp. 214 – 215, October 1985.

*Case report*

# Familial omphalocele

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Accepted 1st July 1985.

An omphalocele is an extrusion of the intestine and other abdominal contents through the umbilical ring. The prevalence rate varies with the methods of ascertainment. McKeown et al,[1] in Birmingham in 1941-1951, found a prevalence rate of 1 in 3,200 live- and stillbirths, and in 1982, in Northern Ireland, the figure was 1 in 2,000 live- and stillbirths.[2] It is usually sporadic, and familial occurrence is rare. DiLiberti,[3] who reported a family with five affected individuals in four generations, could identify only eight previous reports of familial occurrence. We report a family with seven affected persons in four generations. Although there was no male-to-male transmission, the congenital abnormality in this family probably has an autosomal dominant mode of inheritance.

## FAMILY HISTORY

The family, from Ghana, now living in Northern Ireland, was referred for advice on the management of the omphalocele (Figure). In addition to the three affected children of the proposita, there were three other affected relatives. The proposita (III.7) had an omphalocele about 10 cm in diameter covered with skin. She had no symptoms of obstruction or other congenital abnormalities; in particular, there was no macroglossia or visceromegaly. Surgical intervention was unnecessary. She and her husband were not consanguineous. Her eldest daughter (IV.1) aged 8 years had an omphalocele measuring 1.5 cm in diameter. This abnormality was present at birth and, according to her mother, in the past few years had become smaller. The proposita's other two children, dizygotic female twins (IV.2 & IV.3), each had an asymptomatic omphalocele 2 cm in diameter. None of the three children

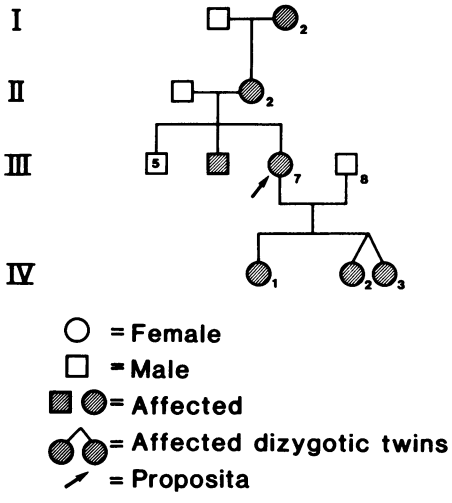


Figure. Pedigree of the family.

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(IV.1-3) had any clinical symptoms or other congenital abnormality. The proposita's brother (III.6) and mother (II.2) were not available for examination, but each was said to have an omphalocele. The maternal grandmother (I.2) who was deceased also had had an omphalocele.

## DISCUSSION

Omphalocele is usually a sporadic congenital abnormality affecting approximately 1 in 3,000 to 1 in 2,000 total births.[1,2] Familial occurrence is unusual. Only nine families have been documented with two or more affected relatives.[3] DiLiberti[3] described a family in which two sisters had an omphalocele, and their father, paternal grandfather, and paternal great-grandfather, had an umbilical hernia. Of the eight other families reported in the literature[3] two also showed the abnormality in several generations.[4,5] Havalad et al[5] described a family with four affected males in a pedigree pattern suggestive of X-linked inheritance. In the six remaining families,[3] the abnormality affected only sibs or half-sibs. Our family is similar to that of DiLiberti[3] with seven affected individuals, one male and six females, in four generations. It has been postulated that in familial cases of omphalocele there may be an inherited defect in muscle or connective tissue.[3] Inheritance in our family is probably as an autosomal dominant trait with variable penetrance although X-linked dominant inheritance cannot be excluded. In counselling parents of a child with an isolated omphalocele, although the overall recurrence risk in sibs is small (under one per cent),[6] it is worth remembering that, occasionally, the abnormality may have a genic origin and be associated with a high risk of recurrence.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 216 – 217, October 1985.*

*Case report*

# Sub-serosal necrosis of the colon in acute pancreatitis

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Accepted 5th August 1985.

As the treatment of acute pancreatitis is mainly conservative, the incidence of colonic involvement following this condition is unknown. Rarely, complications of stenosis, necrosis and fistula formation arise. We report a case in which torrential venous haemorrhage occurring three days after the onset of traumatic pancreatitis necessitated laparotomy. At operation a right hemicolectomy was performed, as her ascending and transverse colon appeared necrotic. Histologically the necrotic process was limited to the sub-serosal layer of the bowel.

***Case History.*** A 29-year-old female was admitted with a three-day history of severe abdominal pain following a blow to the upper abdomen received during the course of a domestic argument. On examination she was shocked, pulse 140 per minute and blood pressure 95/60 mmHg. Marked abdominal distension was present with generalised guarding and rebound. Bowel sounds were absent. Her white cell count was 2,200 per 100 ml and serum amylase 1200 Somygi units. Erect X-ray of the abdomen revealed a distended proximal colon and a 'sentinel loop' adjacent to the pancreas. Free fluid was evident in the pelvic cavity. A diagnosis of acute pancreatitis was made.

Despite conservative treatment, the degree of shock increased and laparotomy was undertaken. A haemoperitoneum in excess of one litre due to haemorrhage from a vein in the lesser omentum was found, and the vein ligated. The surrounding tissues were grossly thickened and inflamed due to reaction from the adjacent haemorrhagic pancreatitis. No further exploration in this region was undertaken because of the risk of further bleeding. The small bowel and descending colon were normal. However, the transverse and ascending colon appeared necrotic necessitating right hemicolectomy. Technically this was difficult due to the greatly thickened mesocolon also involved in the extensive inflammatory process. Post-operatively she had a stormy recovery and required drainage of a large wound abscess. She was discharged at three weeks and six months later remains asymptomatic with no evidence of colonic dysfunction or pancreatic insufficiency.

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Examination of the resected colon revealed multiple areas of haemorrhagic necrosis and saponification in the mesocolon and subserosal surface of the bowel consistent with involvement from an adjacent pancreatitis. Although thrombosis occurred within several small vessels, the major vessels remained patent. There was no evidence of necrosis or ulceration in the muscle coat, submucosa or mucosa of the bowel.

## DISCUSSION

Arterial haemorrhage is a recognised complication following pancreatitis. Its occurrence in association with pseudo-cyst and abscess formation have been reported.[1, 2] Recently, uncomplicated massive intra-peritoneal arterial haemorrhage was described by Lawrie.[3] A comprehensive search of the literature revealed only one case of massive venous haemorrhage occurring in relation to a pancreatic abscess. The reported case is unusual in that venous haemorrhage occurred three days after the onset of haemorrhagic pancreatitis, presumably of traumatic origin. Slow enzymatic erosion of the omental vessel wall or initial thrombosis of the bleeding vessel may explain the delay in onset.

Colonic involvement following pancreatitis has been described. Complications of stenosis, necrosis, spasm and fistula formation have been reported.[4, 5, 6, 7] The mechanism by which these complications arise is not clear. Meyers, Evans and Lukash[8, 9] subscribed to the theory that inflammation spreads from the pancreas between the layers of the transverse mesocolon, giving rise to pericolitis. In the case reported, trauma may have contributed to the appearances described.

This case is unusual in that, while laparotomy was life-saving, it might not have been necessary to resect the damaged area of bowel. We would suggest that those compelled to undertake laparotomy in the presence of acute pancreatitis should be aware of the possible findings. Fortunately this situation does not often arise as the treatment of pancreatitis in this country is mainly conservative. If laparotomy is performed and the surgeon is confronted with what appears to be a necrotic colon, palpation of the mesenteric vessels and careful inspection of the bowel for signs of viability should be undertaken. If doubt still exists, then endoscopic inspection of the mucosa via an enterotomy might be performed.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 218 – 220, October 1985.*

*Case report*

# Ovarian failure in a young woman with galactosaemia

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Accepted 1st July 1985.

Classical galactosaemia is an autosomal recessive condition characterised by an inactivity of galactose –1– phosphate uridyl transferase. This results in elevated levels of galactose and its metabolites which have been associated with damage to the lens, liver, brain and renal tubule. Only recently has it been appreciated that the ovaries may also be affected.

The patient described in this report was treated for galactosaemia from six weeks of age and investigated at 17 years with primary amenorrhoea. This patient demonstrates an unusual cause for hypergonadotrophic hypogonadism, namely galactosaemia, and is thought to be the first reported in Northern Ireland.

***Case History.*** The patient presented at age four weeks with abdominal distension secondary to ascites and hepatosplenomegaly. She was not jaundiced. Reducing sugars were detected in her urine and the diagnosis of galactosaemia was confirmed by finding low levels in the erythrocytes of galactose –1– phosphate uridyl transferase (0.04 units/g Hb, normal range 14·25 units/g Hb) and an intermediate value in her parents (7.76 units/g Hb and 5.14 units/g Hb in mother and father respectively). A lactose-free diet was started at age six weeks.

At age 17 she was referred to the gynaecological endocrine clinic complaining of primary amenorrhoea. On examination she was 160 cm tall, weighed 50 kg, had stage 1 breast development,[1] stage 2 pubic hair development[1] and infantile external genitalia. Serum gonadotrophins were high (LH 50U/1, FSH 85U/1) and serum oestradiol was below the detection limit for the assay (60 pmol/l). This pattern of hypergonadotropic hypogonadism was demonstrated on three occasions indicating ovarian failure as the cause of her hypogonadism. At

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laparatomy there was a small uterus and normal fallopian tubes with bilateral streak ovaries. Histological examination of one complete ovary showed ovarian stroma and a small group of hilar cells. No follicles were present.

## DISCUSSION

In the last few years reports have appeared describing ovarian failure associated with galactosaemia.[2, 3, 4, 5] This is not an invariable association since normal pregnancy in galactosaemic women has also been well documented.[3, 5, 6, 7] Galactosaemia is usually diagnosed in the first few days of life with feeding difficulties, diarrhoea, dehydration and a variable degree of jaundice. Our case was rather unusual, presenting at four weeks of life with abdominal distension due to ascites. This atypical presentation allowed a greater post-natal exposure to galactose than usual. The appearance of the ovarian biopsy in this case was similar to that of a streak ovary, no follicles being detected. It is not possible to say if this represents failure of ovarian development or regression of developed follicles. Kaufman et al showed an increased incidence of ovarian failure with increasing age at the time of diagnosis, suggesting that galactose or one of its metabolites has a direct toxic effect on the ovary and that early treatment may therefore improve the prognosis.[3] There is experimental evidence that this is so, since a toxic effect on ovarian development has been seen in animals fed a high galactose diet.[8] However, Steinmann et al were unable to show an association between age at the time of diagnosis and ovarian failure and suggested that self-intoxication by endogenously produced galactose may lead to ovarian damage.[9] They reported one child who subsequently developed ovarian failure even though she had apparently never been exposed to galactose in utero or in post-natal life. Robinson et al reported a case of hypergonadotrophic hypogonadism in a galactosaemic patient who was commenced on a galactose-free diet at birth.[10] Ovarian biopsy in this case revealed only a reduced number of primary follicles. These observations suggest that ovarian damage due to galactose may have occurred in utero. The authors, however, do not comment on the patients' dietary adherence and there remains the possibility that post-natal exposure to galactose may have occurred.

Alternative mechanisms of ovarian failure have also been suggested. Since the carbohydrate moieties of normal gonadotrophins contain galactosamine and galactose, it has been suggested that ovarian damage may be due to a structural aberration of either LH or FSH in the galactosaemic patient.[3] However, this seems unlikely since gonadotrophins appear to have normal bioactivity in galactosaemic patients.[3] The consensus of evidence is that ovarian damage is related to exposure to galactose. In order to reduce the risk of toxic damage to the ovaries and other tissues in pre-natal and post-natal life, galactose consumption should be avoided by those known to be at risk of conceiving a galactosaemic infant. Even with this precaution, one case of ovarian failure has been reported[9] and we must therefore await further evidence before the value of galactose restriction can be definitively stated. However, at present, the evidence is such that those females with normal ovarian function who either have galactosaemia or are known carriers, should be made aware of the risk to their offspring and should maintain a strict lactose-free diet while at risk of conception. This may reduce the risk of fetal ovarian damage and subsequent failure. Strict compliance to a lactose-free diet for female galactosaemic children should be advised from birth. Galactosaemic females with primary amenorrhoea should be screened promptly to exclude gonadal failure.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 221 – 223, October 1985.*

*Case report*

# Duodenal rupture complicating childhood non-accidental injury

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Accepted 5th August 1985.

Duodeno-jejunal flexure injury is well recognised in blunt abdominal trauma generally. It is usually caused by compression of the relatively fixed bowel against the spine producing a shearing force which tears the bowel.[1] Non-accidental injury is a rare cause of duodeno-jejunal flexure injury in childhood, but serious complications can ensue if there is a delay in diagnosis, which unfortunately is common with this form of injury.

***Case Report.*** A three-year-old boy was admitted as an emergency, with a twenty-four hour history of lethargy, vomiting and upper abdominal pain. Shortly after admission he developed hypovolaemic shock and was immediately resuscitated. There was no sign of external trauma and on abdominal examination he had generalised peritonism. Radiographs revealed a large amount of free gas under the diaphragm and a healing fracture of the left seventh rib. His mother denied any history of trauma. It was learned later that he had been admitted twice in the last year, once with a fractured skull and cracked ribs, and again with failure to thrive and soft tissue bruising. As no adequate explanation could be found to account for the child's medical condition a case conference was called. Following this his name was put on the local 'at risk' register but this decision was later reversed at a further meeting because of improved family circumstances.

Subsequently a laparotomy was performed when gross peritonitis was found secondary to a 75 per cent circumferential tear at the duodeno-jejunal flexure. Associated with this was a three-centimetre rent in the lesser omentum not involving the structures at the free edge and a small haematoma in the right lobe of the liver. The bowel was repaired in two layers with end to end anastomosis and peritoneal lavage carried out. Post-operatively his wound burst on the tenth day and required to be sutured again, prolonging his recovery. Eventually at discharge seven weeks later he was thriving again without abdominal complaint. Shortly after his admission to hospital his father admitted assaulting him and criminal proceedings followed.

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## DISCUSSION

Over the last twenty years since Kempe[2] first described the battered child syndrome an increasing spectrum of specific injuries has been described. Soft tissue and skeletal injuries were noted initially, visceral injuries later, and most recently sexual abuse has been highlighted. In child abuse, in contrast with the pattern of visceral injury from other causes,[3] gastro-intestinal injuries are more frequent than those to solid organs.[4] There are 15 well-documented cases of small bowel perforation in association with child abuse, approximately half of which involved the duodeno-jejunal flexure region, shown in the Table.

TABLE

*Documented cases of small bowel perforation in association with child abuse*

| *Investigator* | *No. of cases* | *Sites of trauma* |
|---|---|---|
| McCort, Vaudagna[5] | 7 | duodenum + jejunum |
| Touloukian[6] | 2 | duodeno-jejunal flexure |
| Tank[7] | 1 | jejunum |
| Gornall, Ahmed, Jolleys, Cohen[4] | 1 | duodeno-jejunal flexure |
| O'Neill[8] | 1 | jejunum |
| Grosfield, Ballantine[9] | 1 | ileum + duodenum |
| Woolley, Mahour, Sloan[10] | 2 | duodenum |

Perforation in this part of the bowel is due to a shearing force produced by a sudden de-acceleration injury tearing the bowel at the anti-mesenteric border close to its point of attachment to the posterior abdominal wall.[1] In non-accidental injury the force is usually the result of a parent's punch or kick. The mortality of visceral perforation due to blunt abdominal trauma in other settings has been reported at 16-20%,[7] whereas in child abuse some small series have reported a mortality of up to 50%.[5, 6] Early diagnosis is thought to be the most significant factor in limiting mortality because surgical management is simple at this stage i.e. primary closure. The diagnosis, however, may be complicated in child abuse and consequently delayed. In the cases reported, all the children were under three years of age, precluding an independent history. Parents often delay seeking help for the child and may actually deny any trauma.[8] This means that the diagnosis is dependent on physical signs. These may be overlooked due to attention being drawn to frequently associated more obvious limb fractures and head injuries. The latter may also mask physical signs if the level of consciousness is seriously depressed.

Visceral trauma may also be the sole manifestation without evidence of external trauma. X-rays are also generally unhelpful as free gas is only found in a minority of cases.[1] Three of these features were common to this case. The recent literature suggests this to be a rare type of injury with no reliable non-invasive aid to early diagnosis. A surgeon must retain a high index or suspicion of visceral trauma in any 'at risk' child with an abdominal complaint.

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*The Ulster Medical Journal, Volume 54, No. 2, pp. 224 – 228, October 1985.*

*Case report*

# The first heart transplant patient from Northern Ireland

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Accepted 4th September 1985.

A 27-year-old bricklayer was admitted to the South Tyrone Hospital, Dungannon, in August 1984. He gave a two-week history of shortness of breath and cough productive of green sputum. He had no chest pain, paroxysmal nocturnal dyspnoea, orthopnoea or peripheral oedema. He was a non-smoker and drank 12 pints of beer per week. He was pyrexial (temperature 99.8°F) and dyspnoeic at rest. He had a cough productive of blood-streaked sputum. The pulse was 132/minute regular. Jugular venous pressure was not raised and the blood pressure was 90/70 mmHg. First and second heart sounds were normal. There was a third heart sound at the apex but no murmurs. In the chest there were coarse and medium crepitations bilaterally in both mid and lower zones.

White cell count was $11,000 \times 10^6$ per litre (73% neutrophils, 27% lymphocytes) and ESR 55 mm in the hour. Chest X-ray showed generalised cardiomegaly and the lung fields showed pulmonary oedema. There were also patchy areas of consolidation throughout the lung fields. ECG showed sinus rhythm, rate 130/minute with a normal axis: PR interval was normal, left ventricular and left atrial hypertrophy were present and there was T wave inversion in V3 to V6. Blood gases showed $PO_2$ 52 mmHg and $PCO_2$ 22 mmHg. Echocardiography showed dilatation of the left atrium and left ventricle with reduced contractility in the posterior wall of the left ventricle. All valves were normal and there was no pericardial effusion. The picture was consistent with dilated cardiomyopathy. Antibodies to coxsackie, adenovirus, cytomegalovirus, psittacosis, Q fever and mycoplasma were not raised. Sputum culture was negative.

The diagnosis was left ventricular failure secondary to dilated cardiomyopathy caused by a possible myocarditis in view of the short history and clinical and echocardiographic findings. There was an associated chest infection.

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***Management***

He was treated with digoxin, diuretics and vasodilators and warfarin. Despite negative sputum cultures, broad spectrum antibiotics were given and also a short course of high dose steroids. There were runs of self-limiting ventricular tachycardia for which he was started on mexiletine orally.

His condition improved clinically and radiologically and he was gently mobilised. Five days after discontinuing corticosteroids he became acutely breathless and developed a mitral regurgitant murmur with a cough productive of frothy sputum indicating left ventricular failure. Prednisolone was recommenced (60 mg daily), the diuretics continued and within 24 hours there was clinical and radiological improvement. He remained stable for the next four weeks and was discharged home. Over the next three months he required three further admissions for treatment of left ventricular failure.

In December 1984 he was transferred to the Royal Victoria Hospital for further investigation. Cardiac catheterisation and myocardial biopsy were performed and the results of cardiac catheterisation are shown in the Table. Endomyocardial biopsy examination by light and electron microscopy showed the features of a cardiomyopathy. The myocardial fibres were in disarray with a variation in fibre diameter; there was considerable variation in nuclear size, and mitochondrial aggregates were found within the interstitium. There was no inflammation, fibrosis or amyloid deposits. There were no features present on which to make an aetiological diagnosis.

TABLE

*Cardiac catheterisation data*

| *Site* | *Pressure (mmHg)* | |
|---|---|---|
| Right atrium | a | 21 |
| | v | 17 |
| | mean | 14 |
| Right ventricle | Systolic | 53 |
| | End diastolic | 10 |
| Pulmonary artery | | 49/31 |
| Pulmonary wedge | a | 32 |
| | v | 39 |
| Left ventricle | Systolic | 89 |
| | End diastolic | 32 |
| Aorta | | 89/61 |
| Left ventricular ejection fraction | | 13% |

*Angiography*

Left ventricle: Markedly enlarged. Contraction very poor, all wall movements uniformly reduced. Some mitral regurgitation into enlarged left atrium

Right ventricle: Markedly enlarged and contracted poorly. Marked tricuspid regurgitation present.

Conclusion: Congestive cardiomyopathy.

His subsequent course was one of progressive congestive heart failure despite digoxin, intensive diuretic and vasodilator therapy. He required inotropic support (intravenous dobutamine infusion) and despite these measures his cardiac function continued to deteriorate. Progressive hyponatraemia and uraemia developed. The only chance for survival appeared to be cardiac transplantation and he was transferred to Papworth Hospital, Cambridge, in February 1985 for assessment for transplantation. As he was so ill from a low cardiac output state a 'red alert' was circulated for a donor heart. A suitable donor became available on 22 February 1985.

### *Operative and Post-Operative Course* (Papworth Hospital, Cambridge)

The donor heart was implanted and defibrillated from ventricular fibrillation into sinus rhythm. This was followed by a short period of complete heart block. Isoprenaline infusion was maintained for five days and atrial pacing continued for 14 days. On stopping the atrial pacing, the heart maintained normal sinus rhythm at a rate of 75 to 80 per minute.

Pre-operatively he was given cyclosporin A and azathioprine, but because of deterioration in renal function post-operatively cyclosporin A was discontinued and he was maintained on azathioprine. He received corticosteroids at first intravenously and then orally until day 10 when the steroids were stopped and cyclosporin A recommenced. The azathiaprine was continued. There were no rejection episodes in the first two months.

As renal function had deteriorated prior to operation, he had to be dialysed whilst on cardiopulmonary bypass. Post-operatively he again had deteriorating renal function necessitating change in his immunosuppressive therapy. On day 10 his renal function started to improve and on discharge his blood urea was 9.7 mmol/l. He was transferred from the intensive care unit to the general ward on day 17 post-operatively. He had a gradual convalescence and was discharged from hospital on the 54th post-operative day. He returned home and has continued convalescence there without complication. His cardiac function is now Grade I (New York Heart Association).

### *Pathology of the Resected Heart*

The heart weighed 405 gm. All four valves were normal. Both ventricles were dilated, the right ventricle measuring $5 \times 3 \times 8$ cm and the left ventricle measuring $7 \times 8$ cm. The coronary arteries were normal. Microscopically there were wavy myocytes and there was moderate hypertrophy of the myocytes in the left ventricle. In the left ventricle there were some areas of contraction bands and two foci of lymphocytic and eosinophilic infiltration in the lateral and septal walls. There was no fibrosis or amyloid present. The findings were consistent with a congestive cardiomyopathy.

## DISCUSSION

The first human-to-human heart transplantation was performed in Cape Town in December 1967.[1] Since then, several hundred patients have undergone cardiac transplantation in 22 countries throughout the world, the largest centre being at Stanford, California. The primary indication for cardiac transplantation is severe cardiac failure unresponsive to conventional therapy and due to irreversible disease of the myocardium of the left ventricle. The patient should be 15 to 50

years with a stable social and psychiatric background, with no active or chronic chest infection and no insulin-dependent diabetes or recent pulmonary infarction.

The donor should be between the ages of 15 and 35 years, with no history of cardiac disease, systemic infection or extracranial malignancy. All donor hearts used in the Papworth programme have been removed at the referring hospital by a surgical team from the transplant unit. The diagnosis of brain death in the donor and the maintenance of ventilation and haemodynamic stability of the donor patients are the responsibility of the referring clinicians. The donor heart is removed, rapidly cooled and stored in cold cardioplegic solution at 2-4°C and transported to Papworth, the desirable upper limit of transit being four hours.[2] During the five-year period January 1979 to December 1983, 62 hearts were used from a total of 250 offers.[2] Seventy-seven were rejected on medical criteria, and 80 hearts were not used because of insufficient local facilities.

The recipient is placed on cardiopulmonary bypass. For orthotopic transplantation as in our patient the heart is excised leaving the posterior walls of both atria and their venous connections in situ. The aorta and pulmonary artery are divided immediately distal to the aortic and pulmonary valves. The donor atria (including the sino-atrial node) are sutured to the corresponding structures in the recipient,[3] as are the aorta and pulmonary artery.

Heterotopic transplantation as performed by Barnard since 1974 now involves biventricular bypass, with anastomoses between recipient and donor right atriae, left atriae, aortae and pulmonary arteries. Heterotopic transplantation carries the potential advantage of leaving in situ the recipient's own right ventricle which is often healthy or may be hypertrophied in response to raised pulmonary resistance. The recipient's own heart may also provide support for the circulation while the donor heart function is compromised by transit-induced ischaemia or acute rejection. The overall survival rates at one, two and three years for heterotopic transplantation were 64%, 50% and 40% respectively.[1]

Rejection is most frequent in the first three months with an average frequency during this time of one episode per 22 patient days, decreasing to one episode per 325 patient days after the first year.[3] The aim is now to detect activation of the immune response system by immunological monitoring using sheep red cell rosette formation and endocardial biopsy before rejection has become established.[4, 5] Chronic rejection is an insidious process which obliterates the donor coronary arteries, and is assessed by annual coronary angiography. The incidence of graft arteriosclerosis at Stanford has improved since the introduction of anti-thrombotic agents, with a graft arteriosclerosis rate of 35% in five years.[4] Seventeen out of 27 patients transplanted at Papworth from 1977 to 1981 were alive at the end of 1981,[3] and 50 out of 94 patients operated on at Stanford between 1973 and 1978 survived four years.[4] In terms of quality of life, 90% of patients transplanted at Stanford up to August 1976 and surviving three months post-transplantation returned to New York Heart Association Grade I. The development of malignant neoplasms in transplant recipients has been recognised since 1968,[6] particularly among those with renal transplants. During the follow-up of 141 patients with heart transplants from Stanford between 1968 and 1977 malignant neoplasms developed in 11 patients. The time interval from transplantation to diagnosis of malignancy ranged from 135 days to 78 months.

At 1982 prices the estimated cost per patient transplanted at Papworth, including pre-operative assessment and first year post-operative follow-up is of the order of

£15,000.[3] The major component of this bill is the cost of post-operative surveillance for rejection and infection. If an immunosuppressive 'magic bullet' were available — effective but non-toxic — the cost of heart transplantation could be reduced to little more than the cost of routine open heart surgery. From 1979 to 1983, 40% of patients selected for transplantation died whilst waiting for a heart to become available.[2] An adequate supply of donor hearts requires awareness by intensive care clinicians that the need exists, and their willingness to ask for the organ to be donated. Out of a total of 250 offers concerning cardiac donation, only on 19 occasions was consent withheld by relatives,[2] and many hearts were offered by relatives agreeing to donation of kidneys, and then asking if other organs could also be donated. Transplant teams acknowledge the difficulty in asking distressed relatives for permission to transplant organs, but feel justified by the benefit which other patients stand to gain.

Human cardiac transplantation, either orthotopic or heterotopic, has been performed in several hundred patients in 22 centres throughout the world. It offers an increase in survival and improved quality of life to those with terminal cardiac failure for whom conventional therapies are ineffective. So far two patients from this province, both with congestive cardiomyopathy, have had successful transplants. Success of the procedure depends on an awareness among clinicians throughout the country — both that such a facility exists for suitable patients, and that a demand exists for a steady supply of suitable donor hearts.

We are grateful to Mr Terence English and Mr Richard Cory-Pearce for permission to publish details of this case, and to Mrs Caroline O'Reilly for typing the manuscript.

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**Handbook of neonatal intensive care.** (Second edition). By Henry L Halliday, Garth McClure and Mark Reid. (pp 333. £7.50). London: Baillière Tindall, 1985.

Following the great success of the first edition of this book four years ago, the rate of change in the field of neonatal intensive care has been so rapid that this revision is necessary. It is an essentially practical book, and the authors have therefore included recommendations for nursing as well as medical management. It is aimed primarily at junior medical staff, who are rightly exhorted to consult their seniors when in doubt. I suspect that if the seniors have any doubt they would turn to this manual which contains a great deal of information in a highly accessible form. There are numerous tables and charts, and a particular feature of the book is the large number of clear diagrams whose scope ranges from labelled drawings of equipment in common use through illustrations of practical procedures to schematic representations of chest radiographs and echocardiograms.

There is no other handy volume which covers the same field in this detail, and it is hard to think of one which would do it better. It will undoubtedly run into many more editions. JAD