Volume 69 No. 1 **MAY 2000**
ISSN 0041-6193

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THE ULSTER MEDICAL JOURNAL

Published by
THE
ULSTER MEDICAL SOCIETY

The Ulster Medical Journal, Volume 69, No. 1
May 2000

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The Ulster Medical Journal, Volume 69, No. 1, May 2000.

The Ulster Medical Journal

The Journal of the Ulster Medical Society. First published in 1932.
Successor to the Transactions of the Ulster Medical Society (1884-1929), and the Transactions of the Belfast Clinical and Pathological Society (1854-1862)

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THE ULSTER MEDICAL JOURNAL

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The Ulster Medical Journal, Volume 69, No. 1, May 2000.

Editorial

A breastfeeding strategy for Northern Ireland

The word "breastfeeding" is not listed in the index of the *Ulster Medical Journal.* The majority of the province's medical students and post-graduate trainees in obstetrics, paediatrics and general practice receive no training in the practical management of breastfeeding.[1] These omissions both reflect and contribute to public attitudes to breastfeeding in Northern Ireland.

Only 45% of infants born in Northern Ireland receive any breast milk and within eight weeks half of these will be fully artificially fed;[2] we share with the Republic of Ireland the lowest breastfeeding rate in the world.[1] The recently published *Breastfeeding Strategy for Northern Ireland* from the Department of Health and Social Services analyses this situation and offers many practical recommendations.

Artificial infant feeding causes substantial morbidity, some mortality and increased health care costs, even in affluent countries.[3] Infants who receive little or no breast milk are subject to more infections, including gastro-enteritis, respiratory and urinary infections, and acute, recurrent and chronic otitis media,[3] and in later childhood are more likely to be overweight,[4] atopic[5] and diabetic.[3] Preterm infants and those born small for gestational age (SGA) benefit from breast milk in the prevention of necrotising enterocolitis;[3] SGA infants show better catch-up growth (including growth of the head circumference) if fed breast milk.[6] Standard infant formula does not support brain development as well as breast milk, in both preterm and term infants; preterm formulas now include compensatory amounts of long-chain polyunsaturated fatty acids, but the problem remains in other formulas.[3]

Mothers who breastfeed experience both short – and long-term health benefits,[3] including efficient weight loss following delivery and some protection against ovarian and endometrial cancer. The lactational amenorrhoea method of contraception is as effective as barrier methods. Epidemiological evidence suggests that bottle-feeders are more likely than breast-feeders to sustain osteoporotic hip fractures in old age.

The benefits of breastfeeding for mother and infant are dose-related; many only follow several months of exclusive breastfeeding.[3] For this reason, the DHSS recommends exclusive breastfeeding for four to six months, with continued breastfeeding throughout the first year.[3] In Northern Ireland, only 5% of infants are still receiving breast milk at the age of nine months.[2]

Why has Northern Ireland such exceptionally poor levels of breastbeeding? Mothers say they initially choose artificial feeding because they would like other people to help with feeding, because they dislike the idea of breastfeeding, or because of previous infant feeding experiences; the commonest reasons given for early abandonment of breastfeeding are breast pain and perceived insufficient milk supply.[2] These explanations reflect social norms, women's expectations and knowledge of infant feeding and the skills of health professionals in overcoming problems. It is sad to note that 89% of UK mothers who stopped within six weeks reported that they would have liked to breastfeed for longer.[2]

The part played by women's working lives in breastfeeding decisions is complex. In 1995, only 6% of UK mothers gave employment as a reason for planning to bottle feed, while return to work is not a common cause for abandoning breastfeeding until three to four months after delivery.[2]

A striking insight into Northern Irish women's experience of breastfeeding comes from a recent study carried out by the Health Promotion Agency of Northern Ireland, which found that 70% of breastfeeding mothers had never breastfed outside their own homes (HPANI, unpublished). This highlights the predicament of the breastfeeding mother – an isolated figure in a bottlefeeding culture.

The DHSS's *Breastfeeding Strategy* defines its goals and identifies the agents to be held responsible for achieving them. The first three objectives are in the fields of health service planning and management: (a) co-ordinating promotional activities, (b) commissioning support

services and (c) collecting statistics in a standardized format to allow comparisons and calculation of trends over time. Research into poorly understood areas, such as effective approaches for low uptake districts and social groups, is recommended.

The *Strategy* calls for improved and continuing training in lactation management for health professionals, and outlines what is being done already. The nursing professions have already achieved a great deal. Medical undergraduate and postgraduate training in this area, however, remains minimal (a matter of incredulity for nursing colleagues and also for parents of breastfed children). If we are to lead the health service, and indeed the public, in evidence-based practice, we must repair this omission.

The specific benefits of breast milk for the most vulnerable infants are recognized. The *Strategy* recommends more support for breast milk feeding for these infants, including improved training for health professionals working in this specialized area, better information for parents, and the development of milk banking. The opening of Ireland's first human milk bank this summer within Sperrin Lakeland Trust is a significant advance, and will send a powerful message to the general public about the importance of breast milk.

The *Strategy* offers some ideas on improving public awareness, ranging from the production of appropriate promotional materials to developing breastfeeding education within schools. Community support for breastfeeding outside the home is to be encouraged. A scheme for identifying breastfeeding- friendly shops, restaurants and other public places is already under consideration, with the dual aims of raising general awareness and assisting individual mothers.

Infant milk companies market their products vigorously in Northern Ireland, often violating the International Code of Marketing of Breast Milk Substitutes (for example, by marketing follow-on milks, feeding-bottles and teats directly to the public). These practices make artificial feeding appear normal and comfortingly familiar to parents. The *Strategy* recommends that artificial milk promotion should no longer take place within the health care system, and that Boards and Trusts should ensure that their practices comply with the International Code. Again, doctors will need to inform themselves and prepare to review what has been taken for granted: milk company promotional gifts, for example, are no longer acceptable on health service premises.

The *Strategy* names some areas where, in the longer term, legislative change is needed. It mentions the anomaly of milk tokens, which send a message of support for artificial feeding to those socio-economic groups with the lowest levels of breastfeeding. Flexible working arrangements for breastfeeding mothers are discussed, but the *Strategy* falls short of recommending what many mothers would like and certain researchers have already recommended:[7] extended maternity leave to allow prolonged breastfeeding.

The challenges have been identified. The DHSS's *Breastfeeding Strategy for Northern Ireland,* if implemented, will go a long way towards meeting them.

Carol M A Campbell, MRCGP, Clinical Medical Officer.

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REFERENCES

1. Department of Health and Social Services. *Breastfeeding Strategy for Northern Ireland.* Belfast: DHSS, 1999.
2. Foster K, Lader D, Cheesbrough S (Office for National Statistics). *Infant Feeding 1995.* London: The Stationery Office, 1997.
3. Campbell C M A. Breastfeeding and health in the western world. *Br J Gen Pract* 1996; **46**: 613-17.
4. Von Kries R, Koletzko B, Sauerwald T *et al.* Breast feeding and obesity: cross sectional study. *Br Med J* 1999; 319: 147-50.
5. Oddy W H, Holt P G, Sly P D *et al.* Association between breast feeding and asthma in 6 year old children: findings of a prospective birth cohort study. *Br Med J* 1999; 319: 815-9.
6. Lucas A, Fewtrell M S, Davies P S W, Bishop N J, Clough H, Cole T J. Breastfeeding and catch-up growth in infants born small for gestational age. *Acta Paediatr* 1997; **86**: 564-9.
7. Howie P W, Forsyth J S, Ogston S A, Clark A, Florey C du V. Protective effect of breastfeeding against infection. *Br Med J* 1990; **300**: 11-16.

The Ulster Medical Journal, Volume 69, No. 1, pp. 3-13, May 2000.

Singular Beneficence?

Presidential Address to the Ulster Medical Society Delivered on Thursday, 14 October 1999

Robert W Stout, MD, DSc, FRCP, FMedSci

In 1900 Sir William Osler, who was the dominant figure in medicine at the beginning of this century, stated that medicine is distinguished from other professions 'by its singular beneficence'.[1] In the title of this address, a question mark has been added because 100 years after Osler made this comment, it is worth reflecting on whether medicine has lived up to his views, and what future medicine will have in the years to come.

In 1949, Lord Horder, a leading London physician asked the question 'Whither Medicine?' His answer was 'whither else, but straight ahead'.[2] Today, 50 years later, do we know where straight ahead is? It is important to consider where we are going in the next few decades, and most important for those who have responsibility for educating the doctors who will practise in the new century.

What was medicine like at the beginning of this century? Two paintings of the time give us some information. The first, the 'Doctor's Visit' by Thomas Faed, belongs to Queen's University and hangs in the foyer of the King Edward Building at the Royal Victoria Hospital (Fig 1). Painted in 1889, it shows the doctor calling at the home of a patient, a man who is clearly very ill in bed, attended by his wife, with a child nearby. At about the same time, in 1891 Sir Luke Fildes painted the picture entitled 'The Doctor' which hangs in the Tate Gallery. Here the doctor is within the home, the patient is a child, and the family is in attendance. A feature of both these portraits is that the doctor comes to the patient's home, what would now be called 'care in the community'. The doctor does not have a bag full of drugs or a prescription pad. What he has is time to spend with the patient. What would be the picture of the doctor today? The television programme 'ER', is perhaps somewhat theatrical but nevertheless illustrates a public perception of medicine. The doctors are young, full of enthusiasm, surrounded by high technology, with, as a badge of office, stethoscopes around their necks.

Fig 1. 'The Doctor's Visit' by Thomas Faed, painted in 1889. This painting is part of the Queen's University of Belfast collection and hangs in the King Edward Building of the Royal Victoria Hospital.

Medicine has advanced enormously in the last century, particularly in the last 50 years and what it can now do for patients is unrecognisable compared to what Osler would have written in his textbook. Nevertheless there is what Le Fanu has described as a fourfold paradox.[3] Medicine has never been more powerful in its ability to deliver care and yet:

- doctors are less professionally fulfilled
- the public is neurotic about its health
- alternative medicine is on the ascendancy
- there is an explosion in health service costs

TUBERCULOSIS

Tuberculosis is a disease which has had a prominent role, not only in medicine, but in our

culture and our history.[4] Many of those in the world of art, literature and music have themselves succumbed to this disease and have also used tuberculosis as a theme in their work. It also has an interesting connection with the specialty of geriatric medicine. The rise in the need for specialist facilities for ill and disabled elderly people happened to coincide with the decline in the need for hospital care for patients with tuberculosis as effective treatment became available. As a result many of the sanatoria became geriatric units and some of the pioneers in geriatric medicine were originally tuberculosis specialists. It is interesting to speculate on how this coincidence has influenced the development of the geriatric specialty.

Tuberculosis is a disease which was known in antiquity and is surrounded by mythology. It has had a wide variety of names throughout the years. Perhaps the best known is 'consumption'; it was also known as the 'white death' because of the pallor often associated with the disease and of the treatment, and in John Bunyon's phrase as 'the captain of the men of death'.

KEATS

Three writers, who were also doctors, died of tuberculosis – Schiller at the beginning of the last century, and Chekhov at the end. In between these was Keats[5] (Fig 2). John Keats in fact took very little interest in medicine. Indeed he composed one of his best sonnets 'Much have I travelled in the realm of gold' while attending a lecture on the pathology of the liver. The first real knowledge that he had tuberculosis was when, after a fit of coughing one night, he found his pillow covered in blood. Keats had to endure a great deal of suffering, including the ritual journey to Italy. When he arrived there he had the misfortune to come across an English doctor, who, looking at the emaciated, pale, coughing young man hardly strong enough to stand, decided that there was no physical illness, that it was all in his mind and that what he needed was exercise. He died in 1821, aged 26. His great contemporary, Shelley, who was not medical, also suffered from tuberculosis but was drowned in a boating accident before he could succumb to the disease.

Fig 2. John Keats. Stipple engraving by C W Wass, 1841. Wellcome Institute Library, London.

What is striking was the immense suffering that Keats underwent, much of it the responsibility of the doctors of the time. Sir George Pickering, a recent Regius Professor of Medicine in Oxford, has stated that 'the history of medicine is a monument to human folly'. In Keat's time the standard treatment for any condition was bleeding. Keats was bled until he was practically unconscious. The more blood he coughed up, the more he was bled. A most striking example of this folly is the account of a major-general during the battle of Waterloo who came across a severely wounded soldier being attended by a young doctor.[6] His first thought was to marvel at the devotion of the doctor attending a wounded soldier while under fire, but when he looked more closely he discovered to his horror that the soldier had a huge wound in his thigh from which his femoral artery was gushing blood at a great rate, while the doctor was trying to find a vein in the soldier's hand in order to squeeze out some more blood.

MODERN MEDICINE

Can we be sure at the end of the 20th century that we still don't have treatments that we administer by custom rather than by thought? Sir David Weatherall, the current Regius Professor of Medicine at Oxford, and a most distinguished haematologist, in an editorial with the title 'The Inhumanity of Medicine'[7] has commented that patients with cancer are often subjected to the most intensive protocols of chemotherapy, some of which require them to be taken to death's door in an attempt to eradicate their tumours. But this is what is currently believed to be the most effective way to manage these diseases; in almost

every field of modern high technology patch-up practice, patients are pushed to the extremes of their endurance, and not always for reasons that include a careful appraisal of what is meant by quality of life. One hundred years hence we may look back on this in the same light as we do on bleeding today.

PERCUSSION

At this time, however, some important medical advances occurred which have survived to the present day. The names of the people concerned are largely forgotten. The first is Leopold Auenbrugger [8] (Fig 3). Auenbrugger's father ran an inn, and Leopold had a musical ear, and probably from watching his father tapping the flasks of ale to detect whether they were empty or full, he developed the clinical technique of percussion. In this way he was able to detect, for example, tuberculous cavities and pleural effusions. What Auenbrugger described was direct percussion, in which the fingers were tapped on the chest wall. Corvisart, the most fashionable doctor of the time, adopted this technique and devised the pleximeter, a small disc made of silver or bone, usually with an ornate handle, which was placed on the surface of the chest, and this in turn was tapped with the finger. A further advance was made by an English physician whose name has been lost in history. He came to percuss a patient in Corvisart's clinic, discovered that he had forgotten to bring his pleximeter with him, and being not only forgetful but also innovative, he used the finger of his left hand in its place. Hence the method which we still use today was devised. Medicine is a very conservative profession. Even such a familiar technique as percussion was controversial in its time. Auenbrugger was moved to say 'it has always been the fate of those who tried to improve their arts or sciences to be beset with envy, malice, hatred, detraction or calumny'. He could have added 'or to be ignored'.

Fig 3. Leopold Auenbrugger and his wife. Wellcome Institute Library, London.

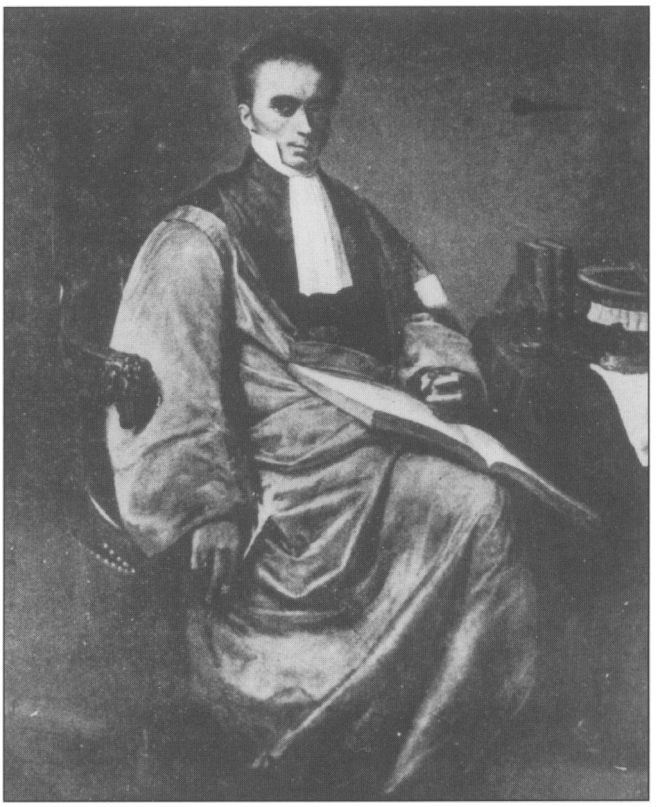

Fig 4. Rene Theophile Hyacinthe Laennec. Reproduction of painting. Wellcome Institute Library, London.

THE STETHOSCOPE

One of Auenbrugger's near contemporaries was Rene Theophile Laennec[9] (Fig 4). Laennec is one of the major figures of the last century, an intellectual genius, who himself died from tuberculosis. Laennec is remembered for the development of the stethoscope. The story is well known, whether true or not. The sounds of the heart or the lungs, if listened to at all, were heard by the physician placing his ear directly on the chest (Fig 5). It is said that Laennec had a patient, a young, beautiful aristocratic woman, and as he was embarrassed to put his ear to her chest, he took a piece of paper, rolled it up into a tube, and listened. The truth appears to be that it wasn't so much the lady's aristocratic birth but her plumpness that impeded Laennec and that it wasn't

Fig 5. Direct auscultation. Wellcome Institute Library, London.

to keep himself at a distance from her that he rolled up the piece of paper but because he was aware that sounds often were transmitted better by a piece of material. Of course, since then the stethoscope has become not only an essential diagnostic tool, but the badge of office of doctors everywhere. Until the second world war, nurses were not allowed to take blood pressure because that required the use of the stethoscope and the stethoscope was regarded as an exclusively medical skill. It wasn't simply the invention of the stethoscope for which Laennec's reputation developed, but because of the use he made of it to explore disease.

CLINICAL SKILLS

Two hundred years later percussion and auscultation are still regarded as essential clinical skills and medical students continue to struggle to acquire them in their introductory clinical course, and now in the Clinical Skills Education Centre. Indeed medicine must be one of the few professions in which skills learnt as a young student and which were first developed two hundred years ago, are retained as core skills throughout a professional lifetime.

But is this right? Have we not advanced in the last 200 years? Few doctors today, certainly those working in hospital, would ever diagnose a chest condition without at least an x-ray, or a cardiac murmur without an echocardiogram. Obstetricians and midwives until recently used a stethoscope similar to Laennec's to listen to the fetal heart but have now moved to electronic means; physicians however continue to rely on their ears and a piece of tubing. Are we simply wasting the time of our patients and our own? What is surprising is how little evaluation there has been on the accuracy and reproducibility of clinical examination. It is surely time for basic clinical skills to be properly evaluated. The results of studies that have been carried out are not reassuring – clinical examination of the chest is only about 50% accurate.[10] There is of course a ritual to the clinical examination, a type of bonding between the doctor and the patient which should not be dismissed, and a physical examination does have a screening function. Physical signs also illustrate pathology and are useful for teaching. But if we are honest, how many of us actually find the signs after we know the diagnosis? It is time that we reviewed the exact place of physical examination in the care of patients, and decided what is useful, what is superfluous and what is frankly misleading. Do we have so little confidence in our role as doctors that we cannot discard some of the rituals of our profession?

THE BRONTËS

The Brontës have a Northern Ireland connection. Their father, the Rev Patrick Brontë, was brought up near Rathfriland and went to Cambridge University, which must have been a remarkable achievement at that time. He settled in Yorkshire at Hawarth where he reared his family in austere circumstances. There were in fact six children, five girls and one boy. The girls were sent to a ghastly boarding school which formed the basis of Lowood School in Charlotte's 'Jane Eyre', where almost certainly they became infected with tuberculosis. Two of the girls, Maria and Elizabeth, died of the disease at the ages of 12 and 11. The next to die was Branwell in 1848; three months later Emily died at the age of 29, and very soon after, Ann at the age of 27. Charlotte continued to live in the by now lonely parsonage with her father. In 1854 she married her father's curate but her tuberculosis advanced and she died

at the age of 39 during her only pregnancy. Their father incidentally lived to the age of 89.

VIRCHOW AND PASTEUR

In the second half of the 19th century major advances revolutionised the understanding of management of tuberculosis. The first was Virchow's development of cellular pathology. Virchow was also a politician and had several differences with Bismarck. Bismarck said of Virchow 'he regards politics as an extension of public health'. The second, about the same time, was Pasteur's germ theory of disease which resulted in huge advances in knowledge, and ultimately treatment of infectious diseases.

KOCH

Pasteur of course did not discover the organism which causes tuberculosis. This was the achievement of the German pathologist, Robert Koch[12] (Fig 6). Koch graduated in medicine with honours at the University of Gottingen, a leading medical school at the time, and he went into rural general practice in the small Prussian town of Wollstein. On his 28th birthday his wife surprised him with a present that was to change their lives. She gave him a microscope. The microscope had been developed 300 years before chiefly by Leeuwenhoek. Koch's microscope was by present-day standards a fairly modest instrument of the sort that 10-year-old children might nowadays receive as birthday presents. Koch taught himself microbiological research, improvised techniques, and was meticulous to a fault. As a result of his work he moved from general practice to the Imperial Institute in Berlin. He made an accidental discovery in his laboratory which has striking similarity to the accidental finding in Fleming's laboratory many years later which led to the discovery of penicillin. A boiled potato cut in half had been left uneaten in the laboratory by a careless or perhaps overworked technician. The following morning Koch noticed bead like growths on the cut surface, a whole series of speckles on the potato. It was Pasteur who said 'chance favours the prepared mind'. Koch's prepared mind theorised that each colony represented the multiplication of a single organism and he used this to isolate pure strains of bacteria. He also realised that simply finding what appeared to be an organism in a tuberculous lesion was not enough to prove that the organism caused tuberculosis. He therefore developed the four postulates or conditions under which cause could be inferred. These were:

- the organism must be found in every lesion;
- it should be capable of being cultivated pure outside the body for several generations;
- after pure culture for sufficient length of time, and for several generations, it should be able to reproduce the original illness in laboratory animals;
- the organism can be retrieved from the inoculated animal and cultured again.

Fig 6. Robert Koch, Lithograph, 1891. Wellcome Institute Library, London.

SCIENTIFIC MEDICINE

It is not so much the content of these simple postulates but their style that is important. Koch can be justifiably regarded as the father of evidence-based medicine, one of the new pieces of jargon of this decade. A preferable term is 'scientific medicine'. Scientific medicine has been defined as 'the prevention and management of illness using methods that have been subjected to the same kinds of rigorous experimental, statistical and observational scrutiny that are applied to other branches of science'.[13] Presumably 'scientific' is not used because of the negative public perception of science. Evidence-based medicine must be treated as what it is, the proper scientific approach to the prevention, diagnosis

and treatment of disease, based on sound research, not as a panacea for reducing costs.

The history of medicine is disfigured by the treatment that is meted out to patients based on no evidence or even lacking in common sense. In the treatment of tuberculosis, examples are the use of sanatoria, trips to Switzerland, various surgical devices such as pleurodesis, thoracoplasty, phrenic nerve crush, and many compounds, some of them shortening life or certainly reducing its quality. None of these were based on any evidence whatsoever. Evidence-based medicine is the basis of quality in healthcare. It must, however, be used judiciously in assessing the vast spectrum of care which is delivered. Absence of evidence does not mean that a service or treatment is not effective, just that we do not know. Many aspects of quality of care are difficult or impossible to measure.[14] Those aspects of life – coping with bereavement for example – that are difficult to measure must not become a lower priority than aspects – such as survival or function – that are easy to measure. The first triumphs of evidence-based medicine were the demonstration that doing nothing was better than bleeding, leeches or purging. The application of evidence, usually derived from studies of large groups of subjects, to the treatment of individual patients will remain a challenge to the practising doctor. Epidemiology should take a critical look at some of its methods, in particular the relationship of biological significance to borderline statistical significance in studies of very large populations. Scientific medicine will remove the distinction between orthodox medicine and alternative medicine – there will simply be medicine that works and medicine that doesn't.

RÖNTGEN

At the end of the century Rontgen (Fig 7) discovered X-rays[15] and this resulted in huge advances in diagnosis and treatment. Pasteur and Röntgen were responsible for advances in medicine, which are as well known to the general public as to doctors, but neither was medically qualified. Pasteur was a chemist and Röntgen a physicist. There are many other examples of scientists contributing greatly to medical knowledge. This is likely to be an increasing feature of future medical advances. However, science has become so complex and so specialised that it is impossible for the average doctor to keep up with, let alone advance, the scientific basis of medicine.

Fig 7. W C Röntgen, Professor of Physics at Giessen, Wuerzburg and Munich, discoverer of X-rays. Wellcome Institute Library, London.

MEDICINE AND SCIENCE

A question for the years to come is the relationship between science and medicine and where doctors fit in, both in medical practice and medical research. The major role of the doctor is the application of scientific advance to the diagnosis and treatment of disease. In order to do this doctors must understand the scientific basis of medicine, but clearly no doctor can be at the leading edge of physics, chemistry and biology, or even any one of these. Likewise scientists must be aware of the possible medical applications of their work. Some would suggest that recent curricular reforms in medical education have removed science from the course and replaced it by topics such as communication skills and ethics, although nobody would question the importance of these. There are even those who suggest that a scientific education need not be a prerequisite for entry to medical school. Yet if doctors cannot at least understand the scientific basis of medicine, how are they going to practise effectively to the benefit of their patients? One answer to this dilemma would be for medical education to become a graduate subject. Before entering medical school the student would take a primary degree. Some might take a degree in advanced science, others for example might take an

American type liberal arts degree, which would include enough science to allow the graduate to understand the scientific basis of medicine. Modern modular degrees provide scope for imaginative degree pathways. This would then be followed by the medical course, which would be shorter than our current five year curriculum, and may well be taken at a different university. The standard North American course, where graduate medical education is the practice, is four years, although the University of Calgary has a three-year medical course. Such a change in medical education might not only have the advantage that the doctor could study in detail a subject, other than medicine, it might also help widen access to medical education, and might allow better means of selection to university on behalf of both the medical school and the aspiring doctor. There would of course be complex financial implications to such a change but they should not prove insurmountable. This is one of the challenges which medicine must face and must tackle soon.

SPECIALISED HOSPITALS

One of the features of tuberculosis was the development of specialised hospitals. In London four specialised hospitals were developed in the last century, the oldest and best known being the Brompton Hospital, founded in 1842.[16] The Brompton nominally had 300 beds but for most of the 19th century, at least half of the beds were regularly empty because of lack of funds or lack of nursing staff, or both. Sir William Whitla in his presidential address to the British Medical Association meeting in Belfast in 1909, noted that the Royal Victoria Hospital had 300 beds, of which only 266 were occupied and the Mater Hospital 150 beds and only 122 occupied.[17]

SPECIALISATION

Tuberculosis, because of its nature and infectivity was always regarded as a specialty and had its own hospitals and medical staff. Indeed until the 1960s there was a lectureship in tuberculosis in the Department of Medicine at Queen's. Tuberculosis must be one of the few specialties if not the only one, which has declined as a result of advances in treatment; the opposite is usually the case. As knowledge advances, as investigation and treatment of disease become more complex, they are best undertaken by doctors who devote their lives and their attention to these particular subjects. Doctors who spend a great deal of their time dealing with particular conditions become more expert at them than those who have less experience. This of course has implications for the organisation of medical care and for the future training of doctors. It also has implications for patterns of care. Is there a future for the generalist? Should we be training generalists or specialists?[18] It seems clear that to have the highest quality in most branches of medicine, specialists are required. However, if we repeat the same question, but change the wording slightly – do we wish to be treated by a generalist or a specialist, the answer is not so clear. Many patients have more than one disease, many diseases affect more than one system in the body, and in any case who is going to select the correct specialist for the patient presenting with disease for the first time, a very important decision? Another of Osler's aphorisms was 'the good physician treats the disease, great physician treats the patient'.[19] There will be a continuing need for generalists who will take an overview of the whole patient but the exact role of that person, their training and their relationship to the specialists, is still not clear. Whether generalists will themselves also have specialties is also not clear but seems most likely. Generalists of course continue to exist in general practice, in accident and emergency medicine and in care of the elderly. They might be all that are required. The balance between generalists and specialists will be one of the most difficult problems in the future. Clinical governance, appraisal and revalidation will give an added impetus towards specialisation, with all the implications that this will have on staffing a health service which now has the lowest staffing levels in the western world.

RESOURCES

Another issue is the use of resources and the associated word 'rationing'. There is no doubt that some type of rationing is necessary. What needs to be decided is the basis for the rationing and who will administer it. Will it be the doctor, or will it be somebody else? An interesting debate on this issue occurred recently in the New England Journal of Medicine and the British Medical Journal. The editor, now former editor, of the New England Journal, takes the view that doctors should have nothing to do with rationing. 'When patients are sick and vulnerable, they expect their physicians to be their advocates for optimal care, not for some minimalist standard'.[20] Another

Boston physician responded "To be truly excellent clinicians we must love our patients and that makes us want to do as much as possible for each person's health. To be truly responsible citizens, however, we must do as much as possible for the population's health within available resources. This commitment to fairness requires us to embrace priorities and rationing. In the United States we call love for patients fidelity and seeking fairness for the population stewardship. Since priority setting and rationing inevitably deprive identifiable people of potential benefits, the question for practising clinicians is whether they can embrace fidelity and stewardship in their dealings with patients".[21] Richard Smith, editor of the British Medical Journal, goes further and states that 'any system that makes one set of players think about quality and another about cost would experience unresolvable conflict. The better system is to oblige all players to think about quality and cost'.[22] It has been clear for many years that no country in the world, no matter how wealthy, can afford all the medical care that it is possible to provide, nor is it always appropriate in the individual patient to provide all medical care that it is available. The combination of scientific medicine, quality standards and ethical principles should help us address these very difficult issues. Doctors must continue to be advocates for their patients, but must not opt out of their responsibilities as unusually well-informed citizens to advise on the best use of limited resources.

PREVENTION AND TREATMENT

The picture of tuberculosis changed dramatically with the advent of immunisation and then chemotherapy, first streptomycin in 1948 and then the other drugs.[23] The sanatoria started to empty and chest physicians diversified their activities. The disease was conquered. But was it? In 1997 over 7.3 million people developed tuberculosis, and 3 million died of it, more than for any other infectious disease.[24] There are two major reasons for this. One is the increasing number of susceptible people, particularly those suffering from AIDS. About one third of the incidence of tuberculosis in the last five years can be attributed to HIV. The other is the development of resistance to standard treatment.

EQUITY AND GLOBALISATION

Three issues will be important in healthcare over the next few years, quality, resources and equity. Quality and resources have already been discussed. Equity tends to be considered in local terms. A feature of the years to come is what has been described as 'globalisation'.[25] Chris Patten, in his book 'East and West' puts it more dramatically – 'in recent years globalisation has become the five-syllable terror of the political economy'.[26] He goes on to say that 'the notion that what it represents is new is laughable'. In fact globalisation was a feature of the end of the 19th century with huge migrations of population and free trade throughout the world. Globalisation is usually thought of in terms of transfer of information and of money but it ought also to be considered in terms of health and disease. Is it acceptable that 7 million people develop tuberculosis, a preventable and treatable disease? Despite the advent of drug resistance, it is possible to treat the condition and it is merely a question of resources. The resource issues which are discussed in this country are totally different from those in so many parts of the world. Huge amounts of resources are spent to keep alive, sometimes for a very short time and in a poor quality of life, very small numbers of people in western countries, when millions are dying from conditions which could be adequately treated with much less cost. Surely this is unacceptable

Figure 8

HIV/AIDS

1981	First recognised
1983	HIV-I isolated
1985	HIV-2
1985	Zidovudine (AZT)
1986	First trial reported

Fig 8. The Discovery of HIV/AIDS

Figure 9

vCJD

1985	BSE first identified
1986	BSE shown to be a prion disease
1990	'Beef is safe to eat' (repeated 1993)
1995	vCJD first identified
1996	BSE linked to vCJD

Fig 9. The Discovery of vCJD

to a caring profession. We must globalise our notions of equity.

THE CHALLENGES OF SUCCESS

There have been great advances in improving health care, particularly in the western countries, but each new success brings its own challenges.

Speed of Advancing Knowledge

The first is the speed at which knowledge is advancing. Knowledge of tuberculosis has developed over centuries and this has led to at least some degree of control and containment of the disease. Compare this with two modern diseases. AIDS or HIV was first described in 1981.[27] Very rapidly, because of the existence of research laboratories in immunology and other relevant disciplines, its nature was discovered, the virus identified, and treatment, perhaps not yet fully effective, has been developed (Fig 8). This is a justification for so called pure research because if the researchers had not been there, the ability to advance our knowledge of this disease would have been severely curtailed. Curiosity driven research must be encouraged. Indeed, Peckham has challenged us to quote any examples of the success of directed research.[28] Because science attempts to discover what is unknown, it is inherently unpredictable. It should be recalled that research on DNA in the 1950s and 60s, driven entirely by curiosity and with no practical implications in mind, has resulted in the biotechnology industry, the human genome project and new understanding of many diseases. Variant Creutzfeld Jacob Disease was first described only a few years ago and is caused by a totally new type of infectious agent.[29] Knowledge has rapidly advanced but unfortunately there is yet no treatment available (Fig 9). Compared with knowledge of tuberculosis, these diseases have been known for

				Microscope	1660
				Leeuwenhoek	1632-1723
1800	Schiller		d 1805 a 46	Percussion	1772
				Auenbrugger	1722-1809
	Keats		d 1821 a 26		
				Stethoscope	1818
		Maria	d 1825	Laennec	1781-1826
		Elizabeth	d 1825		
	Bronte	Branwell	d 1848	Cellular basis of disease	1858
		Emily	d 1848	Virchow	1821-1902
		Anne	d 1848		
		Charlotte	d 1854	Bacteria	1878
				Pasteur	1822-1885
				Tubercle Bacille	1882
				Koch	1843-1910
				X-Rays	1895
				Röntgen	1845-1923
1900	Chechov		d 1904	BCG	1921
				Calmette	1863-1933
				Guérin	1872-1961
	D H Lawrence		d 1930		
				Streptomycin	1946
				PAS	1948
	Orwell		d 1950	Isoniazid	1952
				HIV/AIDS	1981-1986
				vCJD	1985-1996

Fig 10. Calendar shows on the left some literary events and on the right some major events in the history of medicine.

a tiny amount of time (Fig 10). Future doctors will have to be able to assimilate rapidly advancing knowledge. Our patients will also have access to this knowledge through the Internet so doctors must be able to deal with well-informed patients, perhaps better informed than the doctor at the time of consultation. Patients will have access to medical knowledge without the need for the doctor as an intermediary. This will shift the balance of power from the doctor to the patient.

Ethical Issues

The second challenge of success is the emergence of ethical issues in the application of medical technology. They tend to concern issues surrounding conception at the beginning of life, and issues at the end of life. Ethical issues are not the prerogative of doctors alone, or indeed of professional ethicists. The community as a whole must decide what value it places on prolonging life, as well as the use of resources and other issues, some of which I have mentioned.

Ageing

The third challenge of success is the ageing population. Ageing is not new. It is its extent that is new. One third of everybody aged 65 or over who has existed in the whole history of humankind is alive today.[30] The world population aged 65 and over is increasing by three quarters of a million people per month. In the next 25 years it is estimated that the population aged 65 and over will grow by 88% whereas the working age population will grow by only 45%. Clearly this will have huge implications, not just medical, but on society and the economy and we must be prepared for these. Population ageing has implications for all countries and in the 21st century one of the biggest challenges will be how best to prevent and postpone disease and disability and to maintain the health, independence and mobility of an ageing population. Healthy life expectancy is influenced by a relatively small number of chronic disabling conditions that become more common with increasing age. These must be tackled as high priorities. Knowledge of the human genome and other advances will undoubtedly help in this. The ageing population is a fifth paradox in modern medicine. Despite the huge increase in survival into old age, people seem to be obsessed with death rates from heart disease, cancer and other conditions. While premature death must be prevented, every life is finite. As well as globalisation, Dahrendorf has identified the 'death of utopia' as a characteristic of the end of the 20th century.[25] People, he writes, no longer believe in perfection. This does not seem to be the case in health and medical care.

Change

We are in a period of immense change. Proust has stated that every generation believes that change is happening more rapidly in its generation than in any other. There may be some justification for that statement at the moment. How, therefore can we cope with a rapidly changing subject in a changing world? We have to establish some fixed points around which change can occur. We must go back to the values of medicine[31] and maintain these as the fixed points around which our profession will move with technological and other changes. Of the values, competence is clearly what patients first desire from their doctor. Defining, teaching, assessing and re-assessing competence will be challenges in the years to come. But competence is not enough. A machine could be competent. Communication is clearly important, and caring and commitment are vital.

FUTURE DOCTORS

Each year it is my privilege to present the new medical graduates at the graduation ceremony. I envy those starting their medical careers now. I am well aware of the problems of junior doctors. We take delightful, caring and extremely gifted young people into medical school, we make a huge effort to provide them with a high quality medical education, and then we subject them to enormously long hours, sleep deprivation, sometimes starvation, and substandard accommodation. How is it that on the one hand there is expansion of medical schools to cope with a shortage of doctors, while at the same time many of our brightest young doctors are stagnating in dead-end so-called training posts, or are working as perpetual locums because there are no career posts available. These problems are real and they are a disgrace to the profession. It is time the profession took ownership of these problems. They could be resolved tomorrow if there was the will to do so. Despite all of this I envy our young doctors because I believe that they are entering a period of unparalleled and exciting advances in our understanding and treatment of disease, the best opportunity for beneficence that we have ever had.

THE GOALS OF MEDICINE

'The goals of medicine', Osler stated in 1902, 'are to wrest from nature secrets which have perplexed philosophers in all ages, to track to their sources the causes of diseases, to correlate the vast stores of knowledge so that they may be quickly available for the prevention and cure of disease – these are our ambitions'. These goals are as relevant at the end of the twentieth century as they were at its beginning.

REFERENCES

1. Porter R. The Greatest Benefit of Mankind. A Medical History of Humanity from Antiquity to the Present. London: *Harper Collins* 1997; 630.
2. Horder Lord. Whither Medicine? *Br Med J* 1949; 557-60.
3. Le Fanu J. The Rise and Fall of Modern Medicine. London: *Little, Brown* 1999.
4. Dormandy T. The White Death. A History of Tuberculosis. London: Hambledon, 1999.
5. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon,* 1999; 13-21.
6. Dormandy T. The White Death. A History of Tuberculosis. London: Hambledon, 1999; 15.
7. Weatherall D J. The inhumanity of medicine. time to stop and think. *Br Med J* 1994; **309**: 1671-2.
8. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 27-9.
9. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 32-9.
10. Wipf J E, Lipsky B A, Hirschmann J V, Boyko J, Takasugi J, Peugeot R L, Davis C L. Diagnosing pneumonia by physical examination. relevant or relic? *Arch Intern Med* 1999; **159**: 1082-7.
11. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 101-4.
12. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 129-37.
13. Weatherall D J. Scientific method and the art of healing. In: Weatherall D J, Ledingham J G G, Warrell D A (eds) Oxford Textbook of Medicine, 3rd edition, Oxford: *Oxford University Press* 1996; 7-10.
14. Higginson I J. Evidence based palliative care. There is some evidence – and there needs to be more. *Br Med J* 1999; **319**: 462-3.
15. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 144-6.
16. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon*, 1999; 82-4.
17. Whitla, W. The Belfast Medical School: A survey of the state of medical education: necessary reforms and the Queen's University of Belfast. *Br Med J* 1909, **2**: 249-55.
18. Rhodes J M, Harrison B, Black D, Spiro S, Almond S, Moore S. General internal medicine and specialty medicine – time to rethink the relationship. *J R Coll Physicians Lond* 1999; **33**: 341-47.
19. Porter R. The Greatest Benefit of Mankind. A Medical History of Humanity from Antiquity to the Present. London: *Harper Collins*, 1997; 682.
20. Kassirer J P. Managing care – should we adopt a new ethic? *N Eng J Med* 1998; **339**: 397-8.
21. Sabin J E. Fairness as a problem of love and the heart: a clinician's perspective on priority setting. *Br Med J* 1998; **317**: 1002-4.
22. Smith R. Another editor bites the dust. Trust is needed to balance editorial independence and accountability. *Br Med J* 1999; 319: 272-3.
23. Dormandy T. The White Death. A History of Tuberculosis. London: *Hambledon,* 1999; 363-9.
24. Zumla A, Grange J M. The 'global emergency' of tuberculosis. *Proc R Coll Physicians Edinb* 1999; **29**: 104-15.
25. Dahrendorf R. Towards the Twenty-First Century. In: The Oxford History of the Twentieth Century. Howard M, Louis WR (eds). Oxford: *Oxford University Press* 1998; 334-43.
26. Patten C. East and West. London: *Macmillan*, 1998.
27. Weller I V D, Conlon C P, Peto T E A. HIV infection and AIDs. In: Weatherall D J, Ledingham J G G, Warrell D A (eds) Oxford Textbook of Medicine, 3rd edition, Oxford: *Oxford University Press*; 467-83.
28. Peckham M. Future Health Scenarios and Public Policy. In: Clinical Futures. Marinker M, Peckham M (eds). London: *BMJ Books* 1998.
29. The BSE Story. BSE Enquiry. htp://www.bse.org.uk
30. Life in the 21st Century. A vision for all. World Health Report 1998. Geneva: *World Health Organisation* 1998.
31. Core values for the medical profession in the 21st century. Report of Conference, 3-4 November 1994, British Medical Association.

The Ulster Medical Journal, Volume 69, No. 1, pp. 14-18, May 2000.

A review of 100 consecutive free tissue transfers

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Accepted 4 April 2000

SUMMARY

Following the introduction of microsurgical techniques the availability of free tissue transfer has radically transformed reconstructive possibilities for both oncological and surgical defects. This study is a review of 100 consecutive free tissue transfers (free flaps), carried out in 96 patients over a period of 25 months in our unit. The indications for surgery in this series mainly resulted from malignancy, trauma, chronic osteomyelitis, burns and congenital abnormalities. The tissues transferred included various combinations of skin, fat, fascia, muscle, bone and several free digits. Fourteen cases required re-exploration, of which 12 were salvaged, and the overall success rate was 96%.

INTRODUCTION

The principle of reconstructive surgery is the replacement of lost or deficient tissue with similar tissues.[3] A variety of tissues including skin, mucous membrane, cornea, fat, tendon, bone and nerve may be used as grafts. The essential difference between a graft and a flap is that a graft is a non-vascularised structure which depends on the recipient site for nutrition until a suitable circulation has been established, whereas a flap has an independent circulation from the outset. A free flap consists of tissue perfused through a single vascular pedicle, which is detached from the circulation entirely and subsequently revascularised, by means of a microvascular anastamosis, at the recipient site. This technique facilitates restoration of form, contour and function by transferring tissue with more than one specialised component.

The concept of free tissue transfer has progressed through the initial experimental phase in animals in the 1960's.[4,7,3] In the early 1971 Kaplan transferred a free groin flap, which survived for three weeks.[15] Several authors have subsequently reported cases of free tissue transfer in humans.[5,6,12,13,19,23,24]

One advantage of free tissue transfer is the ability to transport vascularised tissue in a single operation thus avoiding multistage procedures. The independent blood supply also avoids the necessity to rely on the recipient bed thereby facilitating the use of flaps in contaminated wounds, in irradiated areas and over large avascular areas such as bone or foreign bodies. Tissue with specialised function may be transferred to restore sensibility, muscle power, bone or even part of the gastrointestinal tract. The ability to select tissue from a distance spares the limited local resources, which may have been compromised by trauma or irradiation rendering them unsuitable for use.

Disadvantages of free tissue transfer include prolonged operating times with most procedures taking four to six hours and longer in complicated cases. This is kept to a minimum with two teams working simultaneously on the donor and recipient sites. As larger and greater varieties of tissues are used for reconstruction, certain problems such as contour defect, decreased muscle power, sensation and some specialised function is compromised in specific donor sites. These need to be carefully considered against the severity of the reconstructive requirement and the risk of failure.

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Microvascular surgery requires microvascular instruments, magnifying loupes and an operating microscope. These are not too expensive by modern standards especially if there is a large volume of microvascular work carried out in the specialist unit. Apart from the instrumentation microvascular surgery requires considerable training of both medical and nursing staff.

This review of 100 consecutive cases was carried out in order to determine the current incidence of free flap failure and associated morbidity in our unit as compared to results published in the current world literature.

METHODOLOGY

100 consecutive free tissue transfers in 96 patients were reviewed. These had been performed over a period of 25 months by five consultants. Patient demographics, hospital stay, indications, complications and flap survival were analysed. The flaps requiring re-exploration were assessed regarding fate of the flap, subsequent management and the outcome.

RESULTS

There were 65 male and 31 female patients. Two patients had two free flaps simultaneously for bilateral breast reconstruction and two patients required a second free flap following failure of the initial procedure, bringing the total up to 100. Mean hospital stay was 31 days (range 8 to 133).

The majority of the procedures were undertaken for reconstruction of the breast and head and neck following malignancy and for limb defects (Fig 1). There were 9 types of free flap used, the most common of which was the radial forearm flap (Fig 2). Microvascular anastamoses were carried out in either end-to-side or end-to-end orientation, using an interrupted suturing technique with 8/0 or 9/0 nylon. All patients received both intraoperative and post-operative dextran 70 for a period of 5 days.

There were two deaths. Both of these high-risk patients had undergone resection of intraoral malignancies with an associated neck dissection, and the cause of death was sepsis followed by multi-organ failure. Four flaps failed. These included two muscle flaps used following debridement of chronic osteomyelitis of the tibia, one TRAM flap for breast reconstruction and one radial forearm flap used for reconstruction following resection of an intraoral carcinoma.

Figure 1
Indications for surgery

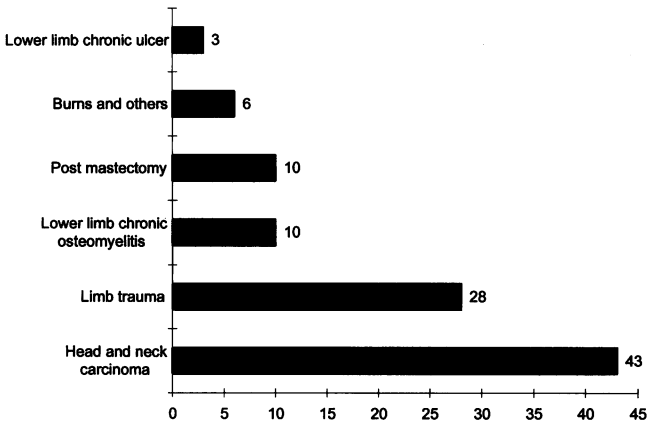
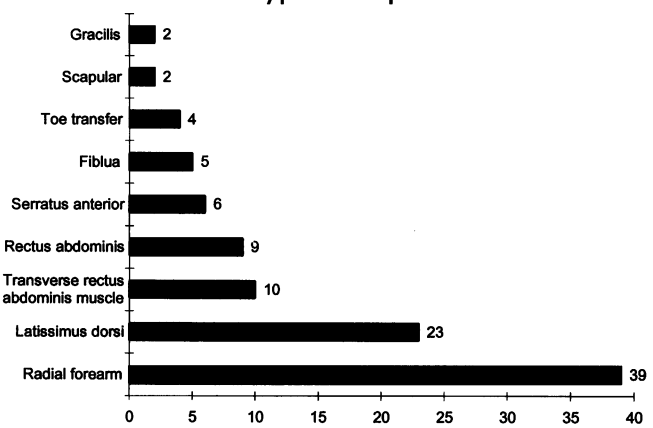


Figure 2
Type of flap



Of the two flap failures in the lower limb, one latissimus dorsi muscle flap failed due to an underlying haematoma and a rectus abdominis flap was lost due to vasospasm of fibrotic vessels. Both patients subsequently were successfully treated with further free latissimus dorsi flaps. A TRAM flap for breast reconstruction following mastectomy failed due to venous thrombosis, and a patient with intraoral carcinoma avulsed his radial forearm flap in the postoperative period whilst profoundly confused due to an episode of delirium tremens.

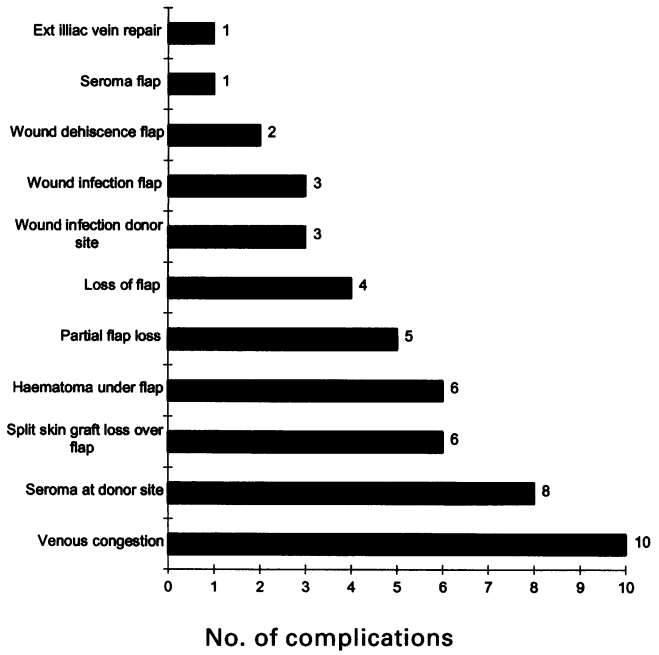
14 flaps required re-exploration (Table I). Of these 12 were salvaged. Seven required evacuation of haematoma, four venous anastamosis were redone due to thrombosis and one required a second venous anastamosis. Two of the 12 salvaged flaps required both evacuation of haematoma and revision of the venous

TABLE I

Flaps re-explored

Flap Type	*No. of flaps*	*Venous thrombosis*	*Haematoma*	*Removal of sutures*	*Flap lost*
Radial forearm	7	3	4		
TRAM	5	1	2	2	1
Latissimus dorsi	1		1		1
Gracilis	1	1			

Figure 3
Flap related complications



anastamosis. Two flaps were salvaged by removal of skin sutures on the ward to relieve venous congestion.

The most frequent flap-related complications are represented in Fig 3.

DISCUSSION

Successful free tissue transfer depends on a multitude of factors. These include preoperative consideration such as patient and donor site selection and appropriate investigations. Per-operative factors include thorough debridement of contaminated wounds, meticulous surgical technique, flap design, team organisation and avoidance of twists, kinks and length discrepancies in the vascular pedicle. Anaesthetic input is of the utmost importance in this type of surgery and such cases should only be undertaken by anaesthetists experienced in this field. Postoperative factors include avoidance of hypovolemia, hypotension, hypothermia, infection, as well as immobilisation of the pedicle and anticoagulant prophylaxis. Postoperative monitoring carried out by experienced personnel and early surgical intervention for flap congestion or ischaemia is essential to keep the salvage rate to the maximum (86% in this series).

The consequences of free flap failure are severe in that a donor site defect has been created with no advantage to the patient and that a further prolonged operative procedure with a second donor site will be required in many cases. In this third decade of free flap surgery the success rates have steadily risen to 95 percent and over. This high success rate has been achieved in specialist units, where a large number of trained microvascular surgeons are carrying out a high volume of work.[1, 16-18, 20] Our results for both flap survival and salvage rates are comparable to previously reported series (Table II).[2, 9-11, 14, 17, 21, 22] At our unit in Belfast there has been a steady increase in cases requiring free flaps. In the year 1998 the number of free tissue transfer rose to almost one per week. Not only are more and more free tissue transfers being carried out, there are increasingly wider indications.

It is worth noting that despite multiple cases developing significant complications, all the patients who had a successful free tissue transfer carried out achieved the reconstructive goal to a standard which could not have been reached using any other technique.

TABLE II

Comparison to other series

Study/Survey	*Ref No.*	*No. of centres*	*No. of flaps*	*Category*	*Failure (Percent)*	*Re-op (Percent)*	*Salvage (Percent)*
Soutar (1986)	22	1	60	Radial forearm flap	10.0	–	–
Irons (1987)	14	1	100	–	15.0	12.0	33.0
Harashina (1988)	11	1	200	–	5.2	6.0	–
Arnez (1991)	2	2	50	TRAM flap	6.0	–	–
Schusterman (1994)	21	1	308	–	5.5	6.8	19.0
Hidalgo (1995)	10	1	60	Fibular flap	1.66	6.66	75.0
Hidalgo (1998)	9	1	716	–	2.0	8.0	70.0
Khouri (1998)	17	23	493	–	4.1	9.9	69.4

CONCLUSION

Microvascular free tissue transfer is a highly specialised technique, with very little room for error. There is a steep learning curve, thus it is not safe to carry out free tissue transfer outside a specialised unit geared specifically for microvascular surgery with multidisciplinary support.

Irrespective of immaculate surgical planning and expertise there wild be occasional and disastrous failures. Close monitoring and early re-exploration is the key to keeping the free flap failures to the minimum. Thus with free flap success rates as high as 96 percent they are a safe and reliable first choice reconstructive option for complex deficits.

ACKNOWLEDMENT

We would like to thank our colleagues in the department for allowing us to include some of their cases in this series.

REFERENCES

1. Arnez Z M. Immediate reconstruction of the lower extremity: an update. *Clin Plast Surg* 1991; **18**: 449-57.
2. Arnez Z M, Bajec J, Bardsley A F, Scamp T and Webster M H C. Experience with 50 free TRAM flap breast reconstructions. *Plast Reconstr Surg* 1991; **87**: 470-82.
3. Barron J N and Saad M N. An introduction to operative plastic and reconstructive surgery: general principles and basic techniques. Ed: 1. *Churchill Livingstone* 1980; **1**: 18.
4. Buncke H J Jr, Schuly W P. Total ear reimplantation in the rabbit utilising microminiature vascular anastamoses. *Br J Plast Surg* 1966; **19**: 15-22.
5. Chang T S. Experience in microsurgery in the People's Republic of China. *J Microsurg* 1979; **1**: 154.
6. Daniel R K and Taylor G I. Distant transfer of an island flap by microvascular anastamoses, a clinical technique. *Plast Reconstr Surg* 1973; **52**: 111-7.
7. Goldwyn R M, Lamb D L and White W L. An experimental study of large island flaps in dogs. P*last Reconstr Surg* 1963; **31**: 528-36.
8. Green G E and Som M L. Free-grafting and revascularisation of intestine. I. Replacement of the cervical esophagus. *Surg* 1966; **60**(5): 1012-16.
9. Hidalgo D A, Disa J J, Cordeiro P G and Hu Q Y. A review of 716 consecutive free flaps for oncologic surgical defects: refinement in donor-site selection and technique. *Plast Reconstr Surg* 1998; **102**: 722-34.
10. Hidalgo D A and Rekow A. A review of 60 consecutive fibula free flap mandible reconstructions. *Plast Reconstr Surg* 1995; **96**: 585-602.
11. Harashina T. Analysis of 200 free flaps. *Br J Plast Surg* 1988; **41**: 33-6.
12. Harii K and Ohmori S. Use of the gastroopiploic vessels as recipient or donor vessels in the free transfer of composite flaps by microvascular anastamosis. *Plast Reconstr Surg* 1973; **52**: 541-8.

13. Harii K, Ohmori K and Ohmori S. Hair transplantation with free scalp flaps. *Plast Reconstr Surg* 1974; **53**: 410-3.

14. Irons G B, Wood M B and Schmitt E H. Experience with one hundred consecutive free flaps. *Ann plast surg* 1987; **18**: 17-23.

15. Kaplan E N, Buncke H J and Murray D E. Distant transfer of cutaneous island flaps in humans by microvascular anastamoses. *Plast Reconstr Surg* 1973; **52**: 301-5.

16. Khouri R K. Avoiding free flap failure. *Clin plast surg* 1992; **19**: 773-81.

17. Khouri R K, Cooley B C, Kunselman A R *et al.* A prospective study of microvascular free-flap surgery and outcome. *Plast Reconstr Surg* 1998; **102**: 711-21.

18. Khouri R K. Free flap surgery: the second decade. *Clin plast surg* 1992; **19**: 757-61.

19. O'Brien B M, MacLeod A M, Hayhurst J W and Morrison W A. Successful transfer of a large island flap from the groin to the foot by microvascular anastamoses. *Plast Reconstr Surg* 1973; **52**: 271-8.

20. Shaw W W. Microvascular free flaps: the first decade. *Clin Plast Surg* 1983; **10**: 3-20.

21. Schusterman M A, Miller M J, Reece G P, Kroll S S, Marchi M and Geopfert H. A single centre's experience with 308 free flaps for repair of head and neck cancer defects. *Plast & Reconstr Surg* 1994; **93**: 472-80.

22. Soutar D S and McGregor I A. The radial forearm flap in intraoral reconstruction: the experience of 60 consecutive cases. *Plast Reconstr Surg* 1986; **78**: 1-8.

23. Taylor G I and Ham F J. The free vascularised nerve graft. a further experimental clinical application of microvascular techniques. *Plast Reconstr Surg* 1976; **57**: 413-26.

24. Taylor G I, Miller G D and Ham F J. The free vascularised bone graft: a clinical extension of microvascular techniques. *Plast Reconstr Surg* 1975; **55**: 533-44.

The Ulster Medical Journal, Volume 69, No. 1, pp. 19-22, May 2000.

The prevalence and types of coronary artery anomalies in Northern Ireland

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Accepted 1 March 2000

SUMMARY

Coronary artery anomalies are uncommon, with a reported prevalence ranging from 0.2% to 1.6%. It is important that those who undertake coronary angiographic procedures are aware of the spectrum of these anomalies. Interventional percutaneous coronary revascularisation procedures are widely used in the management of patients with symptomatic coronary atherosclerosis. The presence of a coronary artery anomaly may make these procedures technically challenging. We have reviewed the Cardiac catheterisation database at the Royal Victoria Hospital, Belfast, and report the prevalence and types of these anomalies.

INTRODUCTION

The prevalence of coronary artery anomalies in the general population varies from 0.2% to 1.6%.[1-3] Although coronary artery anomalies are rare, they may result in symptoms, with the clinical spectrum ranging from chest pain to sudden death. Of interest, Click *et al* reviewed angiographic data from the Coronary Artery Surgery Study and reported that anomalous circumflex coronary arteries had a significantly greater degree of stenosis than that found in non-anomalous arteries in age – and gender-matched patients.[1]

Coronary angiography remains the gold standard in the diagnosis of coronary artery anomalies. The recognition of these anomalies is of particular significance when a patient requires percutaneous therapeutic coronary intervention or cardiac surgery.

The purpose of this study was to establish the prevalence and anatomical patterns of coronary artery anomalies in the adult population of Northern Ireland.

METHODS

This study was carried out at the Regional Medical Cardiology Centre, Royal Victoria Hospital, Belfast. Demographic details of all adult patients undergoing coronary angiography at this centre are recorded on a dedicated Cardiology database. Angiographic procedures are performed by Consultant Cardiologists, including several Visiting Cardiologists, and doctors-in-training (under the supervision of the Consultant staff). After the angiogram has been performed the physician, who has undertaken the procedure, should record the diagnostic findings, including the presence of congenital coronary anomalies, on a separate diagnostic form. This information is then entered on the same database. We analysed the data between the period 1 January 1990 to 15 July 1999. Patients with known congenital heart disease were excluded. 18 189 diagnostic catheterisations involving 14 424 patients were performed. Complete diagnostic coding of coronary angiographic findings was available in

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11 411 patients (79.0%). The diagnostic coding information was incomplete in the other patients, due to a failure of some members of the medical staff to complete fully the diagnostic form.

Two approaches were used – the angiograms from those patients recorded as having a congenital coronary anomaly were retrieved and reviewed by two independent observers (n= 50) or details of the coronary anomalies were obtained from the medical notes (n= 9). In two patients it was not possible to validate the presence of a coronary anomaly as both the angiogram and the medical notes had been misplaced.

The coronary artery anomalies were classified according to a scheme adapted from those suggested by Chu and Cheitlin[2] and Angelini.[4] Congenital coronary anomalies were classifed as: (a) ectopic coronary artery origin, (b) absence of a coronary artery, or (c) abnormal distal connection. Angelini has defined a coronary anomaly as any congenital deviation that is seen in less than 1% of otherwise normal individuals.[4] Absence of the left main trunk (side by side origin of the left anterior descending and circumflex) and separate origin of a conus branch were therefore not included in our analysis, as these have been reported in >1% of otherwise normal hearts.[4] Minor variations in the position of a coronary artery origin (such as 'high take-off') in the right or left coronary sinuses were also not included. However, those patients with an extremely unusual coronary artery origin in the respective coronary sinus, which could not be selectively entered or which required a prolonged search, were included.

TABLE

Congenital Coronary Artery Anomalies

Ectopic Coronary Artery Origin	
Anomalous CX from RCS	27
Anomalous CX from RCA	7
Anomalous RCA from LCS	5
Anomalous LMCA from RCS	2
Anomalous LAD from RCS	1*
Single right Coronary Artery	3
Single left Coronary Artery	1
Posterior location of LMCA in LCS	2
Posterior location of RCA in RCS	1#
Absent Coronary Artery	
Absent CX	4*
Absent RCA	1
Abnormal Distal Connection	
LAD to PA Fistula	4
LMCA to PA Fistula	1
CX to Coronary Sinus	1
TOTAL	60*

* Note: one patient had both an abnormal origin of the left anterior descending coronary artery from the right coronary sinus and an absent circumflex artery.

Note: right coronary artery not selectively entered.

Abbreviations: CX=circumflex, LAD=left anterior descending, LCS=left coronary sinus, LMCA=left main coronary artery, NCS=non-coronary sinus, PA=pulmonary artery, RCA=right coronary artery, RCS=right coronary sinus.

RESULTS

We confirmed the presence of sixty congenital coronary anomalies in fifty-nine patients, giving an estimated prevalence of 0.52%. Thirty-four were male and twenty-five female. The age range was 19 to 82 years. The details of these coronary artery anomalies are summarised in the Table.

Of these fifty-nine patients, forty-eight had an ectopic coronary artery origin, four had absence of a coronary artery (circumflex artery in three patients and right coronary artery in one patient), one had both an ectopic coronary artery origin (left anterior descending coronary artery arising from right coronary sinus) and absent circumflex, and six had an abnormal distal connection. Of the patients with an ectopic coronary artery origin, the commonest anomaly was an anomalous circumflex artery arising from either the right coronary sinus (twenty-seven patients) or the right coronary artery (seven patients) [Figure 1]. Of the thirty-four patients with anomalous circumflex arteries, four had a dominant circumflex. Four patients had a single coronary artery, which supplied all three branches; three had a single right [Figure 2] and one a single left coronary artery. One patient had an absent right coronary artery, with the circumflex artery continuing beyond the crux to supply the territory normally supplied by the right coronary artery [Figure 3]. Two patients had an extreme posterior location of the left coronary artery in the left coronary sinus and in one patient the right coronary artery was not selectively entered,

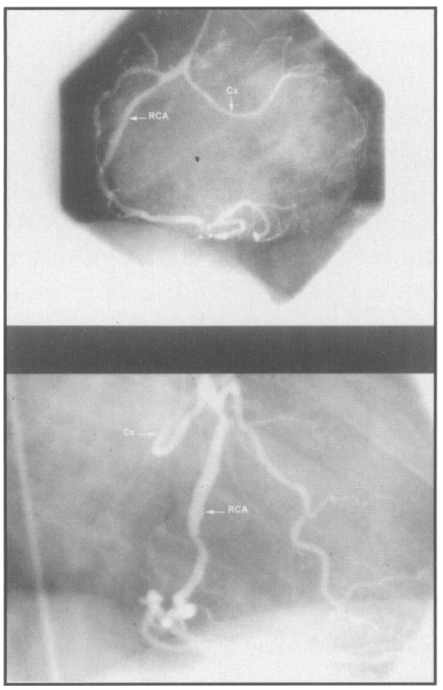

Fig 1. Anomalous origin of circumflex artery from right coronary artery (a) Left Anterior Oblique projection. (b) Right Anterior Oblique projection shows characteristic posterior (retro-aortic) course of the anomalous circumflex artery. Cx=circumflex, RCA=right coronary artery.

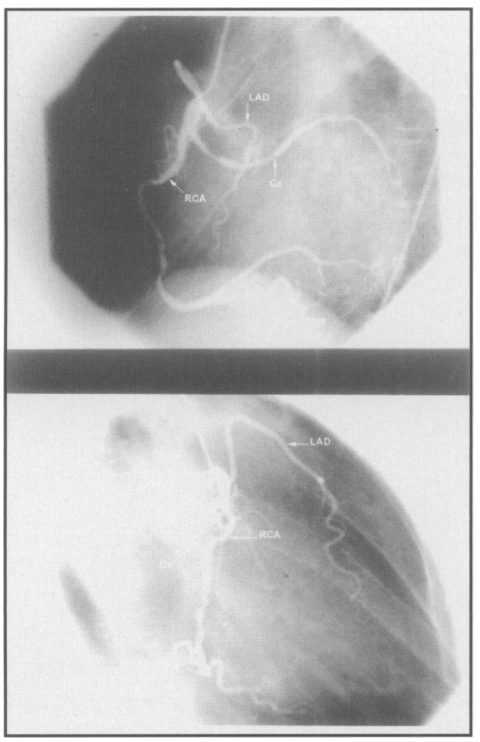

Fig 2. Single right coronary. (a) Left Anterior Oblique projection. (b) Right Anterior Oblique projection. Cx=circumflex, LAD=left anterior descending, RCA=right coronary artery.

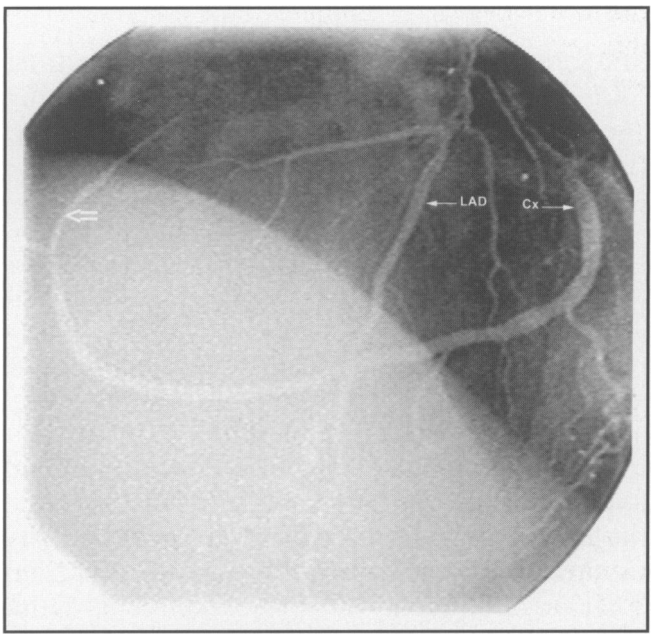

Fig 3. Absent right coronary artery. Left Anterior Oblique projection. The large arrow shows the continuation of the circumflex artery into the territory normally supplied by the right coronary artery. Cx=circumflex, LAD=left anterior descending.

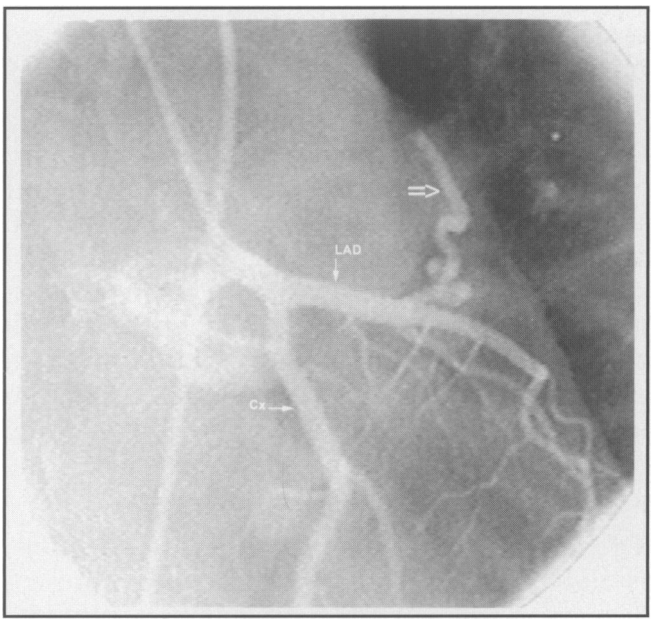

Fig 4. Left anterior descending coronary artery to pulmonary artery fistula. Right Anterior Oblique projection. The large arrow shows an abnormal vessel arising from the left anterior descending coronary artery. On the dynamic images it was clear that this vessel communicated with the pulmonary artery. Cx=circumflex, LAD=left anterior descending.

although on aortography it appeared to have a posterior origin.

Six patients had an abnormal distal connection; four of these were left anterior descending coronary artery to pulmonary artery fistulae [Figure 4].

DISCUSSION

Coronary artery anomalies are rare in adults. Most coronary artery anomalies are not haemodynamically significant and are found incidentally during coronary angiography. One should suspect the presence of a coronary artery anomaly if a myocardial region does not appear to be supplied by any visualised vessel or a vessel appears to cross the aorta and pulmonary artery at the level of the aortic root on left ventriculography or proximal aortic root injection in the right anterior oblique (RAO) projection. This latter appearance is seen with most anomalies of ectopic coronary artery origin from the contralateral sinus or artery.

Coronary angiography remains the gold standard in the diagnosis of coronary artery anomalies, as it is the only method of reliably documenting the course and distribution of the coronary arteries. Angiographic visualisation of the entire coronary circulation is of particular importance in preventing coronary trauma and ensuring optimal revascularisation in patients undergoing coronary artery bypass grafting.

Recent advances in interventional cardiology have resulted in a dramatic increase in the use of percutaneous procedures, often on an urgent basis, for the treatment of both unstable angina and myocardial infarction. The treatment of culprit lesions in coronary artery anomalies is a technical challenge to the cardiologist as early recognition of the anomalous artery is essential in order to minimize time to revascularisation and the procedure (angioplasty and/or stenting of the anomalous artery) itself may be difficult.

The early diagnosis of abnormal distal connections is also important as such patients often present with chest pain. Inappropriate treatment with potent vasodilators may result in a coronary steal phenomenon, thereby exacerbating symptoms, particularly in patients with a left anterior descending coronary artery to pulmonary artery fistula.

In our study we found an prevalence of 0.52% of coronary artery anomalies at angiography. We acknowledge that our angiographic data are incomplete (diagnostic coding available in 79% of patients, and diagnostic validation was not feasible in two patients). However, we believe that our findings are a good reflection of the true angiographic prevalence of these anomalies. Anomalous circumflex arising from the right coronary sinus or the right coronary artery was the commonest coronary artery anomaly in our study. It appears that the range of coronary artery anomalies in the Northern Ireland population is similar to that reported in other angiographic series.[1,2]

ACKNOWLEDGEMENTS

We wish to acknowledge the help and support of all the medical staff undertaking invasive procedures at the Regional Medical Cardiology Centre, Royal Victoria Hospital, Belfast, and the assistance of Margaret Bustard, Senior Systems Analyst, in the provision of data collection and database interrogation.

REFERENCES

1. Click R L, Holmes D R, Vlietstra R E, Kosinski A S, Kronmal R A. Anomalous coronary arteries: location, degree of atherosclerosis and effect on survival – a report from the Coronary Artery Surgery Study. *J Am Coll Cardiol* 1989; **13**: 531-7.
2. Chu E, Cheitlin M D. Diagnostic considerations in patients with suspected coronary artery anomalies. *Am Heart J* 1993; **126**: 1427-38.
3. Kardos A, Babai L, Rudas L, *et al.* Epidemiology of congenital coronary artery anomalies: a coronary arteriography study on a central European population. *Cathet Cardiovasc Diagn* 1997; **42**: 270-5.
4. Angelini P. Normal and anomalous coronary arteries: definitions and classification. *Am Heart J* 1989; **117**: 418-34.

The Ulster Medical Journal, Volume 69, No. 1, pp. 23-26, May 2000.

The Incidence of cardiac lesions in infants born with major gastrointestinal malformations in Northern Ireland

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Accepted 1 February, 2000

SUMMARY

There is a recognised association between major gastrointestinal (GI) malformations and congenital heart disease (CHD). A retrospective study over 10 years involving 240 infants born with gastrointestinal malformations was conducted in the Royal Belfast Hospital For Sick Children (RBHSC). We felt it was important to look at the incidence of CHD diagnosed in the infants presenting to the tertiary referral centre in Belfast. Comparable figures for the incidence of CHD associated with major GI malformations was found in the literature.

INTRODUCTION

The association between major GI malformations and CHD is well recognised. The Royal Belfast Hospital For Sick Children is the regional referral centre for surgery in all infants born in Northern Ireland with major GI malformations. There are about 26,000 live births in Northern Ireland per year. Three hundred new cases of CHD are seen by the paediatric cardiologists, and about thirty infants are born with major GI malformations in the same period. Over the past 10 years all babies presenting with major GI problems have been referred for a cardiological assessment. This paper reports the outcome of that survey.

PATIENTS AND METHODS

All infants referred to the RBHSC with major GI malformations (diaphragmatic hernia, tracheo-oesophageal atresia/oesophageal atresia, anorectal anomalies, duodenal atresia, exomphalos and gastroschisis) between January 1989 and December 1998 were included in the study. All were seen by a paediatric cardiologist, usually prior to GI operation and each patient had an electrocardiogram (ECG), chest X-ray (CXR) and echocardiogram carried out. Since the majority of patients were assessed early in life, many had minor cardiovascular abnormalities, such as haemodynamically insignificant ductus arteriosus, patent foramen ovale and trivial pulmonary artery stenosis. These infants were not included as having a major cardiovascular abnormality.

RESULTS

In total, 240 infants with gastrointestinal malformations were identified over the 10 year period. There were 145 males and 95 females. Average gestation was just over 37 weeks and the mean birth weight 2480 grams. Of these, 37 (15%) had a recognisable syndrome such as Downs and Vater syndromes. Of the total of 240 infants, 53 (22%) had a congenital heart disease (table). Out of the 37 infants with recognised syndromes, a total of 24 (65%) had significant cardiac lesions and of the remaining 203 without syndromes, 29 (14%) had CHD.

The commonest GI abnormality among the infants without recognisable syndromes was imperforate anus (53 cases) and 12 (23%) of these were found to have congenital heart disease. The second commonest abnormality in this group was oesophageal atresia combined with tracheo-oesophageal fistula (32 cases); none had a recognisable syndrome and four (12%) had congenital heart disease.

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TABLE

Distribution of CHD with GI malformations

GI malformations	*No of Infants*	*No(%) with CHD*	*VSD*	*ASD*	*PDA*	*AVSD*	*FT*	*CoAo*	*TGA*	*PA*	*DORV*	*TA*	*Others*
Dia Hernia	35	6(17)		1	3				2				
TOF/OA	48	13(27)	3		3		1	1		1	1	2	Univentricular heart
Anorectal anomaly													
High	12	2(17)	2										
Low	57	14(25)	5	3	1				1	2	1		Hypoplastic left heart
Duodenal atresia	25	13(52)	4	1	1	6							Ebsteins anomaly
Exomphalos	22	4 (19)	2	2									
Gastroschisis	40	1(2)			1								
Total	240	53(22)	16	7	9	6	1	1	3	3	2	2	3

VSD = ventricular septal defect; ASD = atrial septal defect; PDA = Patent ductus arteriosus; AVSD = atrioventricular septal defect; FT = tetralogy of Fallot; Co Ao = coarctation of the aorta; TGA = transposition of the great arteries; PA = pulmonary atresia; DORV = double outlet right ventricle; TA = truncus arteriosus; TOF/OA = tracheo-oesophageal fistula/oesophageal atresia.

Of the total number of infants identified, only one had a family history of GI malformation (anal atresia in a sibling of an infant born with imperforate anus) and four with a positive family history of congenital heart disease, although only two of these were diagnosed as having significant cardiovascular abnormalities.

Fifty-five (23%) of the GI abnormalities were detected on antenatal scanning, the majority being large anterior abdominal wall defects, while only one infant with Downs syndrome and duodenal atresia had an atrioventricular septal (A-V) defect identified in utero.

223 (93%) were seen within the first week of life. Of the remaining 17 children seen after the first week, two had major cardiovascular abnormalities discovered at 10 and 19 days respectively.

Among those infants with known syndromes there was a total of 12 with VATER syndrome, (an acronym for *V*ertebral defects, *A*nal atresia, *T*racheo-*E*sophageal fistula, *R*enal defects and *R*adial anomalies), 15 with Downs syndrome and 10 others. All of the infants diagnosed with VATER syndrome had associated oesophageal atresia and tracheo-oesophageal fistula and five had coexisting imperforate anus. Of the 15 infants with Downs syndrome, the commonest GI abnormality was duodenal atresia in 11 infants, 10 of whom had associated congenital heart disease.

Of those transferred for corrective GI surgery, 42 (17%) of the 240 infants died, eight (19%) of whom had associated syndromes. Of the remaining deaths, five could be attributed to their CHD, while 29 (including eighteen with diaphragmatic hernia) were attributable to major uncorrectable GI malformations.

DISCUSSION

It has long been recognised that there is an association between major GI malformations and CHD; about 20% of patients with major GI malformations have an associated congenital heart defect.[1] In the 1970's, Greenwood *et al* reported the incidence of CHD in infants with a diagnosis of congenital diaphragmatic hernia, imperforate anus, exomphalocele and tracheo-oesophageal

fistula associated with oesophageal atresia to be 23%, 12%, 19.5% and 15% respectively.[2-5] Figures in this paper are 17%, 23%, 19% and 12%.

The recognition of a cardiac lesion in this group of patients is important, particularly in those with associated syndromes. Before embarking on major GI surgery it is important to be aware of the infant's cardiac status both for prognostic purposes and to provide sub-acute bacterial endocarditis (SBE) prophylaxis if appropriate. In a child with coexisting major GI and cardiac abnormality, it may be unwise to proceed with GI surgery. There is also a need to counsel parents regarding risks of future pregnancies. It has long been advocated that echocardiograms should be carried out on these infants as a matter of routine and that clinical examination, CXR and ECG alone, are not adequate to detect all the infants with CHD.[1]

Early reporting by parents of a family history of either CHD or major GI malformations is often sketchy although with an incidence of CHD in the new-born population at about 0.4-0.8%, our results seem to be representative.[7, 8]

Previous studies have revealed a much greater yield in the antenatal detection of large GI malformations compared with cardiovascular abnormalities.[9] Obviously with improvements in fetal ultrasonography, more GI malformations are being detected in utero; this compares to only one cardiovascular abnormality detected on scan in an infant with other congenital abnormalities. This is not surprising, since there is generally less difficulty in identifying large GI abnormalities compared to structural heart defects on antenatal scan. The number of GI malformations detected antenatally in this series appears to be low (only 23%). This may be slightly misleading since this information was taken from the paediatric rather than the antenatal notes. It is an important issue however, since mothers awaiting the birth of a child with a major GI malformation should be transferred to a regional centre capable of carrying out the necessary neonatal surgery.

The importance of early cardiac assessment is seen in the fact that two infants were operated on without echocardiogram and were not thought to have significant CHD (secundum atrial septal defect and a moderate-sized patent ductus arteriosus).

Although the overall incidence of CHD in association with GI malformations in our series of 240 infants was similar to other studies at 22%, the incidence of CHD amongst infants with recognisable syndromes and GI malformations was 65%. Careful examination is essential to rule out the possibility of an associated syndrome in an infant born with a GI malformation and these infants should be scanned early to rule out the high incidence of an associated cardiac defect. A previous study carried out in Belfast showed that infants with Downs syndrome had a 42% chance of having an associated cardiac abnormality, but in our series this is increased to 73% if there is a coexisting GI malformation.[10] This may suggest a greater risk of CHD in Downs syndrome if a GI abnormality is also present. VATER and associated conditions have a high risk of CHD occurring in infants with GI malformations.[1, 11, 12] Again, the infants with VATER association in our series with an incidence of 67% would concur with those previously reported.[13] Only one of the four infants with Beckwith-Wiedemann syndrome was found to have an associated cardiovascular abnormality. Previous studies have shown an association with isolated reversible cardiomegaly but not CHD.[14-17]

Most of the major GI malformations are correctable. The exception are infants with congenital diaphragmatic hernia, known to be associated with high mortality rates.[2, 18-21] Recent overall survival rates by the Congenital Diaphragmatic Hernia Study Group (formed in 1995 with sixty-two centres and 442 patients) was 62%.[22] Of the 35 infants identified with congenital diaphragmatic hernia over 10 years in our study, 17 (49%) survived. The figures for mortality in this paper are, however, not wholly representative, since severe cases with major bowel and cardiac problems never make it as far as the Children's Hospital.

CONCLUSION

This study confirms an increased risk of congenital heart disease among infants with major GI malformations, and particularly amongst those with recognised syndromes. We advocate that infants with major GI malformations should have an early cardiological assessment which should include echocardiogram prior to gastrointestinal surgery and that infants born with such congenital abnormalities should be screened for syndromes and if necessary referred to the genetic service to

enable their parents to be counselled about the potential risk of recurrence in future pregnancies.

ACKNOWLEDGMENTS

We thank Jayne Rodgers, senior echocardiography technician and the paediatric cardiologists. We also thank the parents of children treated at the RBHSC.

REFERENCES

1. Tulloh R M R, Tansey S P, Parashar K, De Giovanni J V, Wright J G C, Silove E D. Echocardiographic screening in neonates undergoing surgery for selected gastrointestinal malformations. *Arch Dis Child* 1994; **70**: F206-8.
2. Greenwood R D, Rosenthal A, Nadas A S. Cardiovascular abnormalities associated with congenital diaphragmatic hernia. *Pediatrics* 1976; **57**: 92-7.
3. Greenwood R D, Rosenthal A, Nadas A S. Cardiovascular malformations associated with imperforate anus. *J Paediatr* 1975; **86**: 576-9.
4. Greenwood R D, Rosenthal A. Cardiovascular malformations associated with tracheo-oesophageal fistula and oesophageal atresia. *Pediatrics* 1976; **57**: 87- 91.
5. Greenwood R D, Rosenthal A, Nadas A S. Cardiovascular malformations associated with omphalocele. *J Pediatr* 1974; **85**: 818-21.
6. Hassinck E A M, Rieu P N M A, Hamel B C J, Severijnen R S V M, Staak F H J, Festen C. Additional congenital defects in anorectal malformations. *Eur J Pediatr* 1996; **155**: 477-82.
7. Rubin J D, Ferencz C, Brenner J l, Neill C A, Perry L W. Early detection of congenital cardiovascular malformations in infancy. *Am J Dis Child* 1987; **141**: 1218-20.
8. Samánek M, Slavik Z, Zbörilová B, Hroboňová V, Voríšková M, Skovránek J. Prevalence, treatment, and outcome of heart disease in live-born children: a prospective analysis of 91,823 live-born children. *Pediatr Cardiol* 1989; **10**: 205-11.
9. Stoll C, Dott B, Alembik Y, Roth M P. Evaluation of routine prenatal diagnosis by a registry of congenital anomalies. *Prenat Diagn* 1995; **15**: 791-800.
10. Tubman T R J, Shields M D, Craig B G, Mulholland H C, Nevin N C. Congenital heart disease in Downs syndrome: two year prospective early screening study. *Br Med J* 1991; **302**: 1425-7.
11. Lubinsky M. Current Concepts: VATER and other associations: Historical perspectives and modern interpretation. *Am J Med Genet* 1986; **2** (suppl): 9-16.
12. Barnes J C, Smith W L. The VATER association. *Radiology* 1978; **126**: 445-9.
13. Weaver D D, Mapstone C L, Yu P-L. The VATER association, analysis of the patients. *AJDC* 1986; **140**: 225-9.
14. Greenwood R D, Sommer A, Rosenthal A, Craenen J, Nadas AS. Cardiovascular abnormalities in the Beckwith-Wiedemann syndrome. *Am J Dis Child* 1977; **131**: 293-4.
15. Nivelon-Chevallier A, Mavel A, Michiels R, Bethenod M. Syndrome de Wiedeman Beckwith-Familial: diagnostic anténatal echographique et confirmation histologique. *J Genet Hum* 1983; **31** Suppl 5; 397-402.
16. Kuehl K S, Kapur S, Toomey K, Varghese P J, Midgley F M, Ruckman R N. Focal cardiomyopathy and ectopic atrial tachycardia in Beckwith Syndrome. *A J Cardiol* 1985; **55**: 1234-5.
17. Ryan C A, Boyle M H, Burggraf G W. Reversible obstructive hypertrophic cardiomyopathy in the Beckwith-Wiedmann Syndrome. *Pediatr Cardiol* 1989; **10**: 225-8.
18. Butler N, Claireaux A K. Congenital diaphragmatic hernia as a cause of perinatal mortality. *Lancet* 1962; **1**: 659-63.
19. Sharland G K, Lockhart S M, Heward A J, Allan L D. Prognosis in fetal diaphragmatic hernia. *Am J Obstet Gynecol* 1992; **166**: 9-13.
20. Allan L D, Irish M S, Glick P L. The fetal heart in diaphragmatic hernia. *Clin Perinatol* 1996; **23**: 795-812.
21. Fauza D O, Wilson J M. Congenital diaphragmatic hernia and associated anomalies: their incidence, identification and impact on prognosis. *J Pediat Surg* 1994; **29**: 1113-7.
22. Clark R H, Hardin W D Jr, Hirschi R B, Jaksic T, Lally K P, Langham M R Jr, Wilson J M. Current surgical management of congenital diaphragmatic hernia: a report from the Congenital Diaphragmatic Hernia Study Group. *J Pediatr Surg* 1998; **33**: 1004-9.

The Ulster Medical Journal, Volume 69, No. 1, pp. 27-29, May 2000.

Episiotomy repair: vicryl versus vicryl rapide

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Accepted 12 January 2000

SUMMARY

Women suffer a significant degree of perineal morbidity in the postpartum period. For some, it can be significant and interfere with daily activities. Although there seems to be no doubt that polyglycolic acid derivatives are superior to non absorbable sutures with regard to wound healing, problems still occur with their use. In this study a relatively new product, Vicryl rapide, was compared with Vicryl.

INTRODUCTION

Episiotomy is the surgical enlargement of the vaginal orifice during labour and delivery and remains a very common operation in obstetrics.[1] The practice was introduced in the 18th century without having strong scientific evidence of its benefits.[2] Its use was justified by the prevention of severe perineal tears, better future sexual function and a reduction of urinary and faecal incontinence. However, no data support any short or long term benefits of routine episiotomy in obstetric practice.[3]

Currently used suture materials are either absorbable or non-absorbable. Absorbable materials include polyglycolic acid, chromic catgut and glycerol-impregnated catgut; non-absorbable materials include silk and nylon. Of the absorbable suture material, polyglycolic acid derivatives (Dexon/Vicryl) degrade hydrolytically, causing minimal tissue reaction and inflammation. However, absorption is not complete until 56-70 days post repair.

A relatively new material, Vicryl rapide (VR), consists of smaller molecules of the same components as coated Vicryl (V) and changes to the manufacturing process give Vicryl rapide its unique characteristics. Vicryl rapide absorbs more quickly than other absorbable materials and absorption is essentially complete by 42 days. At five days post implantation, the tensile strength is reduced by 50% and after fourteen days there is no traction left.

This study was designed to investigate whether mothers with a perineal tear or episiotomy sutured with Vicryl rapide experienced less pain in the post-partum period and less morbidity long-term with regard to wound healing, urinary and bowel habit and sexual function than those patients sutured with Vicryl.

MATERIALS AND METHODS

Women attending the Ulster Hospital, Dundonald, were eligible to enter the trial if they had a parity of 0 to 2, were between 18 and 40 years old, carried a singleton fetus, had a normal vaginal delivery and required an episiotomy, or sustained a second degree tear (skin and perineal muscle). Enrolment took place immediately after delivery and informed consent was obtained. Block randomisation was performed using two sets of sealed envelopes. Questionnaires were completed by the doctor or midwife present at the delivery. All episiotomies were repaired by the same technique using one suture length and subcuticular perineal sutures.[4] All women received a diclofenac suppository (100 mg) per rectum on completion of the repair.

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From 1 February to 31 July 1996, 153 women were recruited into the trial, and of these 118 completed follow-up at six and twelve weeks. Seventy-eight repairs were completed with Vicryl and 75 with Vicryl rapide. In the Vicryl group, 44 patients were primigravid and 34 patients were multiparous; in the Vicryl rapide group, 40 patients were primigravid and 35 multiparous.

All patients were interviewed at 24 hours postpartum, and interviewed and examined on day three. Principal outcomes studied were perineal pain, pelvic floor functioning and wound integrity. Perineal pain was assessed at 24 hours postpartum by patients registering their perception of pain on a visual analogue scale (VAS) and by enumerating all pain medications received during days one to three. On day three perineal pain was assessed using a 4-point scale. At six and twelve weeks, patients were contacted by telephone regarding the resumption of sexual activities and difficulties encountered. The general practitioner or obstetrician performed the six-week check-up with regard to poor healing, infection and residual sutures.

Statistical analysis was performed on these results and means compared using Student's t test. In view of the large numbers, the t-test in such instances resembles a z-test. Thus values of 2.0 or more are as statistically significant as $p < 0.05$.

RESULTS

Using the VAS no difference in perineal pain was noted between V and VR at 24 hours (t-value 0.106). On day three, the type of suture material used created no significant difference in the pain score (t-value 0.813). Prior to discharge, no significant difference in the analgesic requirements between the two groups was noted (t-value 1.259).

However, at six weeks, a significant difference in dyspareunia scores between the two groups was noted. The VR group experienced considerably less pain than the V group. The difference in the mean scores was statistically very significant (t-value 3.854). Thirty percent of patients sutured with V experienced wound problems (infection, gaping wound, pain or residual material requiring removal), compared with 1.7% of VR patients.

At 12 weeks, 20% of V patients had dyspareunia (mean dyspareunia score was 0.27) and only 5% of VR patients complained of dyspareunia (mean score 0.05). This was statistically significant (t value 2.440). Of the 19 patients with wound problems at 12 weeks (infection, gaping wound, pain or residual material requiring removal), 18 were in the V group.

DISCUSSION

A significant number of mothers experience some perineal pain or discomfort in the immediate post-partum period but even months later as many as 20% continue to have problems related to perineal repair.[5] For 10% of these women, problems persist up to one year.[6] Symptoms commonly experienced include short and long term pain, wound infection, wound breakdown and dyspareunia. The choice of suture material has a direct effect on perineal outcome and associated morbidity.[7,8] Grant,[4] concluded that, based on the published experimental data on perineal suturing, the choice of polyglycolic acid for all layers with a subcuticular suture to the skin seemed a preferable policy.

Although there seems to be no doubt that polyglycolic acid is the preferable suture material, there are still problems associated with its use. Coated Vicryl offers effective wound support for up to 30 days and then gradually absorbs. This is longer than would normally be necessary and there is often a need to remove polyglycolic acid material in the puerperium. This may explain why women often experience discomfort and tightness in the postpartum period.

In view of this, we decided to perform this study and ascertain whether mothers sutured with Vicryl rapide experienced less postpartum morbidity than mothers sutured with Vicryl. A similar study by Gemynthe *et al*[9] compared the outcome in those sutured with Vicryl to those sutured with Vicryl rapide. At 48 hours, five days and three months after delivery there was no difference in pain and discomfort in the perineal area between the two groups. At 14 days, mothers sutured with Vicryl rapide experienced significantly less perineal pain and discomfort when walking. The difference in terms of women undergoing removal of stitches or visible stitches at examination two months after delivery was not statistically significant although the rate was higher in women sutured with Vicryl. The difference in pain when walking was explained by the dissimilar tensions at that time which would support the hypothesis based on the physical properties of the Vicryl rapide i.e. at 14 days there is no tensile strength

left whereas in Vicryl there is over 50% tensile strength still present.

In our study no difference was noted in pain levels between the two groups in the initial post-partum period. However, by six weeks those in the VR group experienced considerably less dyspareunia. By 12 weeks the difference between the two groups had diminished but was still statistically significant. Interestingly the average scores in both groups were very small.

Only one patient repaired with VR complained of a wound problem at 12 weeks compared with 18 in the V group. Even assuming that the pain experienced at 12 weeks was not due to the suture material, if this potential bias is fed back to the six week analysis using a regression technique, the difference between the two groups is still very significant.

Our results indicate a clear advantage with regard to decreased incidence of dyspareunia at six weeks in patients sutured with Vicryl rapide compared to those sutured with Vicryl. In addition, with regard to wound problems, our results, although statistically not significant, suggest clinical benefit in those patients sutured with Vicryl rapide.

ACKNOWLEDGEMENT

We would like to thank the patients who participated, the midwives practising in the Ulster Hospital, Dundonald at the time when the study was compiled and Mr Michael Stevenson, Lecturer in Medical Statistics in Epidemiology and Public Health.

REFERENCES

1. Cunningham F G, MacDonald P C, Grant N F *et al.* Williams Obstetrics, 20th edition. *Appleton & Lange, Connecticut*, 1997; **13**: 342.
2. Lede R L, Belizán J M, Carroli G. Is routine use of episiotomy justified? *Am J Obstet Gynaecol* 1996; **174**: 1399-402.
3. Albers L L , Anderson D, Cragin L *et al.* Factors related to perineal trauma in childbirth. *J Nurse-Midwifery* 1996; **41**: 269-76.
4. Grant A. Repair of episiotomies and perineal tears. *Br J Obstet Gynecol* 1986; **93**: 417-9.
5. Sleep J, Grant A, Garcia J, Elbourne D, Spencer J, Chalmers I. West Berkshire perineal management trial. *Br Med J* 1984; **289**: 587-90.
6. Glazener C, Abdalla M, Russell I, Templeton A. Postnatal care: a survey of patients' experiences. *Br J Midwifery* 1993; **1**: 67-74.
7. Mahomed K, Grant A, Ashurst H, James D. The Southmead perineal suture study. a randomised comparison of suture materials and suturing techniques for repair of perineal trauma. *Br J Obstet Gynaecol* 1989; **96**: 1272-80.
8. Ketcham K R, Pastorek J G, Letellier R L. Episiotomy repair: chromic versus polyglycolic acid suture. *South Med J* 1994; **87**: 514-7.
9. Gemynthe A, Langhoff-Roos J, Sahl S, Knudsen J. New Vicryl formulation: an improved method of perineal repair? *Br J Midwifery* 1996; **4**: 230-4.

The Ulster Medical Journal, Volume 69, No. 1, pp. 30-34, May 2000.

Motherhood in the teens and twenties: some surprises

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Accepted 15 March 2000

Summary

We report a study of the association of health and social support variables with motherhood in teenagers and older mothers. Both teenage and older mothers reported poorer physical and mental health and fewer and less frequent social contacts than their nulliparous peers. Contrary to expectation, however, older mothers reported less extensive and less adequate social support networks than did teenagers.

INTRODUCTION

While recent figures show an increase in teenage pregnancies[1,2] and a recent review[3] has suggested that consideration should be given to providing targeted support for teenagers during and after pregnancy, their needs, especially in comparison to those of older mothers have not been clearly identified.[4] Some research evidence suggests that the risk of adverse health and social outcomes for the pregnant teenager may be attributable to social and economic factors rather than to the mother's age[5,6] but the relative contribution of these factors remains controversial. Evidence regarding the health and psychosocial status of both teenagers and older mothers is important to the primary care team in deciding their provision of appropriate health care.[7,8]

The aim of this study was to determine if variables (measures of health and social status) associated with motherhood are the same for teenagers as for older mothers.

METHOD

A cross-sectional case control study design was used to compare four groups (teenage mothers, mothers aged 20-29 years and their respective nulliparous peers) with regard to measures of health, quality of life and social support. Ethical approval was obtained from the local Research Ethics Committee.

Within one five-partner group general practice first time mothers aged less than 30 years, who had one child aged 6-12 months and who lived in housing estates in West Belfast were identified from maternity records. Mothers who had had other pregnancies in the past or who were currently pregnant were excluded from the study sample. Nulliparous females were identified from the practice records and matched with mothers by housing area and age (birth date closest to each mother's). A total of 60 mothers (30 were teenage) and 60 age-matched peers were asked by a partner in the practice for consent to be interviewed by a research worker who was interested in young women's health. With their consent, thirty teenage mothers were recruited within twelve months: a further month was required to recruit an equal number of eligible older mothers.

The health and social status measures used were the Short Form 36 (SF36) Health Survey,[9] Broadhead Social Network Questionnaire[10] and Cantril Ladder[11] and were administered in this order.

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The SF36 assesses respondents' perceptions of physical functional status and well-being. It measures eight different health concepts: scores for each range from 0-100, higher scores representing better health status.[9] It also includes a single item measure of health transition, (range 1-5), in which a higher score indicates that health is worse than a year previously. The Broadhead Questionnaire assesses both the number and frequency of social contacts for the preceding month and expresses these as numeric scores. Satisfaction with these contacts is also measured so that the perceived level of the support (e.g. knowing someone who gives good advice; knowing someone who is interested in them) and the perceived adequacy (e.g. receiving as much care/ affection as wished) of the subject's social network can be evaluated.[10] The Cantril Ladder measures self-assessed health status by asking the subjects to indicate on an illustrated ladder which step they feel represents their state of health currently, in the past (five years ago) and in the future (five years from now). The top of the ladder (step 10) represents the best possible state of health for them and the bottom (step 1) the worst possible.[11] Subjects were interviewed in their own homes. They completed the SF36 themselves but the research worker read out the other questionnaires and recorded responses.

Previous information was not available for accurate estimation of the sample size which was therefore determined by budgetary and time constraints.

Data were entered on to SPSS (for Windows) and analysed by analysis of variance.

RESULTS

The median age at interview for the teenage mothers and teenage nullipara was 18.2 years (interquartile range 0.77) and 18.2 years (interquartile range 0.69) respectively: for the older mothers and their nulliparous peers it was 23.3 years (interquartile range 1.61) and 23.7 years (interquartile range 2.42) respectively.

Analysis of variance of SF36 scores (Table I) indicated significant maternal status effects. Irrespective of age, non-mothers, compared with mothers, had significantly higher scores, which indicated their better health status, in respect of vitality, emotional and physical well-being and mental health. Scores for health transition indicated the extent to which respondents felt

TABLE I

Comparison of effects of age and maternal status: SF36 sub-scales: mean scores and ANOVA

BODILY PAIN

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	80.46	80.53	80.50
Older	72.80	80.30	76.40
	76.63	80.41	

VITALITY

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	47.50	76.00	61.75
Older	46.50	55.16	50.83
	47.00	65.58	

* Main effect: maternal status – F = 6.09; df = 1, 116; p<0.05

PHYSICAL FUNCTIONING

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	91.83	95.16	93.49
Older	89.83	91.50	90.66
	90.83	93.30	

ROLE EMOTIONAL

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	79.96	88.90	84.43
Older	58.10	88.90	73.40
	69.03	88.90	

Main effect: Maternal status – F = 8.85; df 1, 116; p<0.01

GENERAL HEALTH

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	65.73	79.16	72.44
Older	69.70	69.43	69.56
	67.71	72.79	

ROLE PHYSICAL

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	82.00	91.66	86.83
Older	77.66	91.66	84.66
	79.83	91.66	

**Main effect: Maternal status – F = 8.85 1, 116; p<0.01

SOCIAL FUNCTIONING

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	84.30	91.56	87.93
Older	79.00	85.33	82.16
	81.65	84.44	

MENTAL HEALTH

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	56.53	72.13	64.33
Older	59.76	70.60	65.23
	58.14	71.36	

**Main effect: Maternal status – F = 10.55; df 1, 116; p<0.01

HEALTH TRANSITION

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	2.93	2.86	2.89
Older	3.30	2.80	3.05
	3.11	2.83	

N.B. ANOVA applied to all SF36 sub-scales: maternal status, age group and interaction effects not significant except where indicated.

their health was worse currently than it was a year previously. Comparison of these mean scores between mothers and non-mothers reflected a trend that mothers felt that the extent to which their current health was worse was greater; comparison of older mothers' scores with their nulliparous peers suggested that the difference for this age group was greater than that for teenagers.

Table II shows mean scores which reflect the number and frequency of social contacts reported by subjects within the month prior to interview. Mothers, in both teenage and older groups, had smaller numbers of people comprising their social networks than had their nulliparous peers. Moreover, there was an age relationship: older groups reported smaller networks than teenagers.

Also, mothers had less frequent contacts with people in their social networks within the month prior to interview than had their nulliparous peers; the older groups had less than teenagers. The level of support perceived by older mothers was less than that perceived by their nulliparous peers but teenage mothers perceived a higher level of support than did their nulliparous peers. The perceived adequacy of support reported by mothers in both groups was less than that reported by their nulliparous peers: the mean scores of the older groups were less than those of teenagers.

All subjects indicated, on the Cantril Ladder, where they felt their level of health lay currently, five years previously and would lie five years hence: the groups did not differ significantly (Table III). Perceived health status five years previously was better than that perceived currently. All groups, except teenage mothers, expected that their health status would have improved in five years' time.

TABLE II

Broadhead Social Network Questionnaire: mean scores

EXTENT OF SOCIAL NETWORK
(family and friends)

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	56.53	72.13	64.33
Older	59.76	70.60	65.23
	58.14	71.36	

* Main effect: Maternal status – F = 6.31; df 1, 116; p<0.05
* Main effect: Age group – F = 6.55; df 1, 116; p<0.05

SOCIAL CONTACTS IN PAST MONTH

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	25.20	30.56	27.88
Older	21.20	28.63	24.91
	23.20	29.59	

*** Main effect: Maternal status – F = 33.36; df 1, 116; p<0.001
** Main effect: Age group – F = 7.17; df 1, 116; p<0.01

PERCEIVED LEVEL OF SUPPORT

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	17.30	16.80	17.05
Older	14.70	18.30	16.50
	16.00	17.55	

* Interaction effect: Maternal status by age group – F = 5.05; df 1, 116; p<0.05

PERCEIVED ADEQUACY OF SUPPORT

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	21.67	23.03	22.35
Older	18.17	22.07	20.12
	19.92	22.55	

** Main effect: Maternal status – F = 6.97; df 1, 116; p<0.01
* Main effect: Age group – F = 5.01; df 1, 116; p<0.05

N.B. ANOVA applied to all sub-sections: maternal status, age group and interaction effects not significant except where indicated.

TABLE III

Comparison of perceived health status measured by Cantril Ladder – mean scores

CURRENT STATUS

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	6.97	6.70	6.84
Older	6.37	6.80	6.58
	6.67	6.75	

CHANGE FROM 5 YEARS AGO

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	–1.93	–1.23	–1.58
Older	–1.87	–0.70	–1.28
	–1.90	–0.96	

EXPECTED CHANGE IN NEXT 5 YEARS

	Maternal Status		
Age Group	*Mothers*	*Nulliparous*	
Teenage	–0.20	+0.37	+0.09
Older	+0.16	+0.50	+0.33
	–0.04	+0.44	

N.B. ANOVA applied to all sections: no significant effects observed.

DISCUSSION

The design of the study with four groups (i.e. teenage nullipara, teenage mothers, older nullipara and older mothers) allowed assessment of two factors, age and maternal status.

The study only included first time mothers in order to minimise possible confounding factors. It was considered that varying numbers of pregnancies or children could affect maternal well-being and potentially influence measures of health and psychosocial status.

The timing of this study (6-12 months post-partum) was chosen in order to minimise the confounding effects of frequent routine health-care contacts which occur during the first six post-natal months and of other factors which may arise after the baby is a year old.

The results of the SF36 indicate that nulliparous subjects perceived their health to be better overall than did either of the groups of mothers. This suggests that mothers experience poorer mental health, vitality, and emotional and physical well-being than their nulliparous peers irrespective of age.

A previous study which had used the Social Support Questionnaire (which records absolute numbers of identified individuals who provide close social support and subjects' satisfaction with this support),[12] had shown no significant difference between teenage mothers and their nulliparous peers. The Broadhead Questionnaire, used in this study, provides more comprehensive information regarding social networks and types of social activities but does not ask subjects to specify individual relationships. Results obtained using this measure indicate that motherhood, regardless of age, is associated with less frequent social contacts and the social networks of older mothers, rather than of teenage mothers, are perceived as being the least adequate in providing support.

In this study no direct attempt was made to determine the marital status of subjects or whether they were cohabiting, nor were the teenage mothers questioned closely as to whether or not they were still living within the family home. During piloting of the questionnaire prior to the study enquiries on this subject were met with some suspicion. It was felt that detailed questioning could have prejudiced co-operation during the interview since some participants received financial benefits linked to their social (and housing) circumstances. Home and family circumstances, however, are obviously important determinants of social support and networking and further research study is needed in this area. If teenagers were still living within their original families they may have had 'built in' baby-sitting and readily available social support. If older mothers were living in their own homes, perhaps with partners who were out of the home during much of the working day, they may have found practical support less readily available.

The relatively poor perceived health status and social networks of the older mothers were unexpected findings which should be highlighted to those providing health and social care services for this group, particularly members of primary care teams. Since this study included only mothers aged less then thirty, further investigation of these issues with older mothers may be warranted. Despite the current emphasis of concern for young mothers,[13] the level of support provided by her own social network appears to be better for teenagers than for mothers in their twenties. Our results indicate that a first-time mother with a child aged between six months and one year is likely to be disadvantaged in health and social well-being in comparison with her nulliparous peers, regardless of whether she is a teenager or is in her twenties. Further research to elucidate the nature of social support networks for first time mothers, irrespective of their age, would be relevant in addressing this inequality in health.

ACKNOWLEDGEMENT

We wish to acknowledge, with thanks, the funding of this project by the Royal College of General Practitioners and the advice kindly given by Ms Mairead Boohan.

TRIBUTE

Doctors Cupples, Bradley, Irvine and Wilson wish to pay special tribute to Dr Brigid McCann without whose contribution this work would not have been possible. Brigid died in February 2000 after a long illness which she bore with great fortitude. Her continued contribution to life and work in many aspects of the community despite her illness will be greatly missed.

REFERENCES

1. Office of National Statistics. Monitor FM1 98/1. March 1998. Conceptions in England and Wales, 1996. ISSN 1353-5501.
2. Registrar General. 76th Report of the Registrar General N. Ireland: A Governmental Statistical Publication. 1998 Department of Finance and Personel.
3. NHS Centre for Reviews and Dissemination. Preventing and reducing the adverse effects of unintended teenage pregnancies. *Effective Health Care* 1997; **3** (1). University of York. ISSN: 0965-0288.
4. Irvine H, Bradley T, Cupples M, Boohan M. The implications of teenage pregnancy and motherhood for primary health care: unresolved issues. *Br. J. Gen. Pract* 1997; **47**: 323-6.
5. Mackinson C. The health consequences of teenage fertility. *Fam Plan Perspect* 1985, **17**: 132-9.
6. Goldenberg R L, Klerman L V. Adolescent pregnancy – another look. *N Eng J Med* 1995; **332**: 1161-2.

7. Jacobson L D, Wilkinson C E. Review of teenage health: time for a new direction. *Br J Gen Pract* 1994; **44**: 420-4.

8. Jacobson L D, Wilkinson C E., Pill R. Teenage Pregnancy in the UK in the 1990's: implications for primary care. *Fam Pract* 1995; **12**: 232-6.

9. SF36. Ware J E SF.36. Manual & Interpretation Guide 1993, Boston Health Inst., New England Medical Centre.

10. Broadhead W E, Kaplan B H, James A, Wagner E H, Schoenbach V J *et al.* The epidemiologic evidence for a relationship between social support and health. *Am J Epidemiol* 1983; **117**: 521-37.

11. Cantril H. The Pattern of human concerns. New Brunswick, New Jersey. Rutgers Univ Press, 1985.

12. Cupples M E, Irvine H, Bradley T, Boohan M, Reilly P, Patterson C. Teenage mothers and their peers – a research challenge. *Br J Gen Pract* 1998; 48: 1685-6.

13. Teenage Pregnancy. Report of the Social Exclusion Unit 1999.

The Ulster Medical Journal, Volume 69, No. 1, pp. 35-43, May 2000.

Screening for hyperglycaemia in pregnancy: analysis of two screening protocols and review of current methods

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Accepted 12 April 2000

SUMMARY

We assessed the ability of two screening protocols to detect varying degrees of hyperglycaemia in pregnancy and to compare fetal outcome in those found to have normal and abnormal glucose metabolism by either protocol.

493 pregnant women were identified by one of two screening protocols to be at risk of hyperglycaemia in pregnancy.

Pregnancy complications, induction of labour, method of delivery, birth weight, incidence of congenital anomalies and neonatal complications were assessed; there were no significant differences between those with normal and abnormal glucose metabolism detected by either protocol apart from a significant linear trend for the incidence of large for gestational infants with increasing hyperglycaemia in both groups.

Protocol B was as effective in detecting new hyperglycaemia in pregnancy as Protocol A. It involved the use of a breakfast meal profile in the initial assessment of those screened positive, reducing the need for glucose tolerance tests in the vast majority of cases. In the population studied, hyperglycaemia in pregnancy was not associated with adverse fetal outcome.

INTRODUCTION

Hyperglycaemia in pregnancy is a term which can be used to encompass a large spectrum of disordered carbohydrate metabolism, which ranges from the upper end of normality to overt clinical diabetes. Pregnancy has important effects on carbohydrate metabolism, exerted mainly through a decrease in insulin sensitivity, which results in higher post prandial blood glucose levels. In pregnant women with a normal pancreatic ß cell reserve, insulin secretion is increased in response to this decreased sensitivity, and glucose homeostasis is restored.[1] Pregnancy can thus unmask a defect in carbohydrate metabolism in those who have a limited ß cell reserve, resulting in hyperglycaemia of varying severity. Even in present day obstetric practice, hyperglycaemia in pregnancy presents a major risk to the fetus, the effects of which extend from fetal life through neonatal life into adolescence. Hyperglycaemia in pregnancy may damage fetal pancreatic ß cells, increasing susceptibility to carbohydrate intolerance in the future.[2,3]

The aim of screening mothers for evidence of abnormal carbohydrate metabolism in pregnancy is to minimise or eliminate these risks to the fetus. There are a number of screening tests in current use, with no consensus view as to the best method. In the UK the methods more commonly used include clinical risk factors, glycosuria, random plasma glucose and glycosylated haemoglobin. Each of these methods when used alone has relatively low sensitivity and specificity.

The aim of this study was to look at fetal outcome in pregnancies complicated by varying degrees of hyperglycaemia detected by two screening protocols between 1992 and 1996. Those mothers identified by the two screening protocols to have hyperglycaemia in pregnancy, went on to have

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either a 75 g oral glucose tolerance test (OGTT). (1992-1994) or a 300 kcal breakfast meal test (1994-1996). Fetal outcome in those found to have normal and abnormal carbohydrate metabolism by either test, was analysed, in an attempt to ascertain if either test was a 'predictor' for adverse fetal outcome.

PATIENTS AND METHODS

1. Protocol A

Between 1/3/92 and 28/2/94 all patients attending the ante-natal clinic in the Royal Maternity Hospital (RMH) were screened at first booking using 'clinical risk factors' and random venous plasma glucose at booking. In addition all patients had urine tested for glucose at each visit. (Table I). Those mothers with one or more clinical risk factors and/or random venous plasma glucose > 6.6 mmol/1 and/or the presence of glycosuria > + on two or more occasions; had a 75 g OGTT at around 28 weeks (75 g glucose load, taken orally, after an overnight fast, with venous plasma glucose measured at 0, 30, 60, 90 and 120 minutes). Results were interpreted as shown in Table II.

Those patients found to have impaired glucose tolerance using these criteria went on to have a meal profile. This consisted of 'breakfast' and 'lunch' meals, containing 42 g carbohydrate (300 kcal) and 32 g carbohydrate (320 kcal) respectively, with plasma glucose estimated before and two 2 hours after each meal. Results were interpreted as shown in Table III. The meal profile was done in order to assess maternal glycaemic response to normal diet and so determine if treatment was necessary. If a mother had an abnormal meal profile result she was given dietary advice – restricted food intake to 1500-2000 kcal/day, and the meal profile repeated in one week. Only then, if on the diet the result of the meal profile remained abnormal, was insulin treatment considered. If a reading of 11 mmol/1

Table II

WHO criteria for interpretation of GTT

(adapted for pregnancy by "Diabetic pregnancy study group" of the European association for the study of diabetes (1989).

Venous plasma glucose (mmol/l)	*Normal*	*Impaired G.T.*	*D.M.*
Fasting	<6.0	6.0-7.9	≥8
2 hour	<9.0	9.0-10.9	≥11.0

TABLE I

PROTOCOL A	PROTOCOL B
Screening methods:	*Screening methods:*
Clinical risk factors (FH diabetes 1st degree relative, previous baby>4.5 kg, previous unexplained stillbirth or neonatal death, previous fetal abnormality, maternal weight >90 kg.)	Random venous plasma glucose (RVPG) – Booking visit – 28 weeks Urine testing for glycosuria
Random venous plasma glucose (RVGP) – booking visit Urine testing for glycosuria	If RVPG >6.6 mmol/l and/or glycosuria > + on two or more occasions→ Breakfast meal test (as soon as possible) (30% done because of ↑RVPG at booking)
Diagnosis	*Diagnosis*
75 g oral glucose tolerance test (=28 wks) (If clinical criteria and/or RVPG >6.6 mmol/l and/or glycosuria > + on two or more occasions	75 g oral glucose tolerance test (If Breakfast meal test abnormal)
(357 patients screened: 357 had a GTT)	(136 patients screened: 3 had a GTT)

or more was found at any time the patient was diagnosed diabetic and insulin treatment commenced.

In this two year period 378 mothers were identified by the screening protocol to be at risk of hyperglycaemia in pregnancy and had a 75 g OGTT performed; 21 were excluded from further study for various reasons, including multiple pregnancy and vomiting after the glucose load. In total, 357 singleton pregnancies were studied (5.8% of the antenatal population).

TABLE III

Interpretation of Breakfast Meal Test

2 hour glucose:	mean = 5.2 mmol/l
	mean + 2 S.D. = 6.8 mmol/l
	Arbitrary cut-of 8 mmol/l considered abnormal

(Roberts – study of 102 unselected mothers whom had breakfast meal test – 1992 Belfast)

2. PROTOCOL B

Between 1/3/94 and 28/2/96 the screening protocol was changed, so that mothers were not identified to be at risk of having hyperglycaemia in pregnancy purely because of clinical risk factors (Table I). In addition, a decision was taken to test maternal glycaemic response to the intake of normal foodstuffs, only proceeding to formal glucose tolerance testing if this was deemed to be abnormal. During this two year period, all patients attending the antenatal clinic in RMH were screened using random venous plasma glucose at booking at 28 weeks and at any other time if thought necessary by the obstetrician. All patients had urine tested for glucose at each antenatal visit. Those patients with a random venous plasma glucose > 6.6 mmol/1 or the presence of glycosuria on two or more occasions went on to have a breakfast meal test.

The breakfast meal test consisted of a 300 kcal breakfast meal, containing 40 g of carbohydrate – a standard portion of breakfast cereal, two rounds of toast, milk, butter and a cup of tea. It was undertaken after an overnight fast, venous plasma glucose being estimated before and two hours after the meal. Results were interpreted as shown in Table III. For the purpose of comparison with the group of patients found to have IGT by the 75 g OGTT in 1992-94, those patients who had a 2 hr glucose < 8 mmol/1 were subdivided into two groups (1) two hr glucose < 6.8 mmol/1 and (2) two hr glucose 6.9-7.9 mmol/1. Those patients with abnormal results were given dietary advice (food intake restricted to 1500-2000 kcal/day), and the breakfast meal test repeated in one week. If after one week on the diet the breakfast meal test result was still abnormal, as defined above, a 75 g OGTT was performed. A blood glucose of > 11 mmol/1 was regarded as diagnostic of diabetes, and insulin treatment considered. In total, 155 mothers had a breakfast meal test in this two year period, of whom 19 were excluded from further study because of the reasons outlined previously. Therefore, 136 singleton pregnancies identified by the screening protocol in this two year period were studied (2.4% of the antenatal population).

RESULTS

Of the 357 glucose tolerance tests undertaken, 243 (68%) were carried out purely because of one or more positive clinical criteria, 70 (20%) because of glycosuria, and 35 (10%) because of a raised blood glucose (>6.6 mmol/1). Nine patients had a GTT performed for other reasons, which included 'large baby', 'polyhydramnios' and 'obstetrician request' and a number of patients had more than one indication. Of these mothers 12 were found to have impaired glucose tolerance (IGT) and three to have gestational diabetes. The 12 mothers with IGT had a meal profile, four of which were abnormal. These mothers were given dietary advice and none required insulin treatment. Of the three mothers found to have gestational diabetes two were started on insulin and one was treated with diet only.

In total, 136 patients had a breakfast meal test, of which 106 (78%) were carried out because of a random venous plasma glucose > 6.6 mmol/l, 18 (13%) because of glycosuria and 10 for reasons other than these (mainly 'obstetrician request' – because of one or more positive clinical criteria). Of these mothers three were found to have abnormal results. They were all given dietary advice initially. Two mothers had the breakfast meal test repeated; in both cases it was still abnormal and a 75 g OGTT was performed and a diagnosis of diabetes mellitus made. The other patient was admitted to hospital with acute appendicitis before the test could be repeated, and was diagnosed with diabetes while in hospital.

All three patients with abnormal breakfast meal tests required insulin treatment.

Most patients had glycosylated haemoglobin (HbA_{1c}) measured at the time of the GTT or breakfast meal test. The methods used for estimating HbA_{1c} changed twice in the four year period and the results have been adapted accordingly. HbA_{1c} was significantly higher ($p < 0.05$) in those with IGT (3.8%) compared to normal GTT results (3.2%) and in those with abnormal (4.5%) compared to normal breakfast test results (3.5%).

Pregnancy-induced hypertension, pre-eclampsia, urinary tract infection, and polyhydramnios were the commonest antenatal complications, but none was found to be more common in mothers with an abnormal GTT or breakfast meal test. Labour was induced in 150 (44%) of those with normal GTT results, 5 (42%) of those with IGT, and in one gestational diabetic mother (33%). In those who had the breakfast meal test, 52 (39%) with a normal result, and none of those with an abnormal result, had labour induced.

Most mothers with normal GTT and breakfast meal test results had normal vaginal deliveries. Eight mothers with impaired glucose tolerance had a caesarean section, four being elective (previous caesarean section in three patients, and primary infertility in a 37 year old) and four being emergency caesarean sections. A higher incidence of caesarean section associated with impaired glucose tolerance has been reported before.[6] The caesarean section rates for those with normal GTT and breakfast meal test results are similar to the Royal Maternity Hospital overall caesarean section rates for that period (Table IV).

Fetal outcomes for the two groups are shown in Table V. There was no increase in perinatal mortality or incidence of birth trauma in babies born to mothers with abnormal tests in either group. There were no statistically significant differences in birth weight or gestational age at delivery in babies born to mothers with abnormal tests in either group. There was a significant linear trend ($p < 0.001$) in the incidence of large for gestational age babies with increasing hyperglycaemia in both groups. Most babies with congenital abnormalities, major and minor, in the study group were born to mothers with normal GTT or breakfast meal test results. Mean APGAR scores at one and five minutes were similar in those babies born to mothers with normal and abnormal GTT and breakfast meal test results.

TABLE IV

Mode of delivery

	Glucose Tolerance Test			*Breakfast Meal Test*		
	Normal	IGT	DM	Normal (<6.8)	Normal (6.9-7.9)	AB-Normal
	342	12	3	123	10	3
Normal Delivery	226 66%	4 33%	1 33%	73 59%	5 50%	2 67%
Instrumental Delivery	48 14%	0	1 33%	15 12%	1 10%	0
Caesarean Section (total)	67 20%	8 67%	1 33%	35 28%	4 40%	1 33%

	All	IDDM	All	IDDM
Caesarean Section Rate	21%	47%	24%	52%

TABLE V

Fetal outcomes for pregnancies studied by Oral Glucose Tolerance test or Breakfast Meal Test

	Glucose Tolerance Test			*Breakfast Meal Test*		
2 Hour Glucose (mmol/l)	Normal (<9.0)	IGT (9.0-10.9)	DM (>11)	Normal (<6.8)	Normal (6.8-7.9)	Abnormal (>8.0)
No. of Patients	342	12	3	123	10	3
Mean Birth Weight (kg)	3.54	3.79	3.26	3.46	4.04	3.25
Mean Gestational Age (weeks	39.1	38.1	37.3	39.0	39.1	36.7
Large for Gestational Age	72(21%)	6(50%)	1(33%)	22(17%)	4(40%)	2(67%)
Minor Congenital Abnormality	44(13%)	1(8%)	1(33%)	7(6%)	1(10%)	0(0%)
Major Congenital Abnormality	5(1%)	0(0%)	0(0%)	4(3%)	0(0%)	0(0%)

The incidence of neonatal complications known be more common in the infant of the diabetic mother was assessed. There was no evidence to suggest that any of these complications were more common in those babies born to mothers with hyperglycaemia in pregnancy. Most babies who required admission to the special care baby unit were born to mothers with normal GTT or breakfast meal test results.

During the four year period studied, only six cases of gestational diabetes were discovered; three by the GTT and three by the breakfast meal test. Five of these patients were treated with insulin, and all stopped insulin post-delivery. They were all seen subsequently at the Royal Victoria Hospital. Clinical records were traced for four of the five patients, all of whom now have Type 1 diabetes and are on insulin treatment.

DISCUSSION

The aim of screening mothers for evidence of abnormal carbohydrate metabolism in pregnancy is to detect the problem at an early stage and so prevent any adverse fetal outcome. The only meaningful criteria by which to judge the importance of the state of glucose metabolism in pregnancy are fetal outcome, either in the short or longer term, or the long term maternal outcome.[6]

Various indices of fetal outcome have been used to assess the effect of hyperglycaemia in pregnancy. Because of the general decline in perinatal mortality rates in recent years, this index of fetal outcome can no longer be used as a practical outcome measure. Therefore other short term pregnancy outcomes have become more important in assessing the effect, if any, of maternal hyperglycaemia.[7] Maternal hyperglycaemia through its effect on fetal cells, can cause accelerated fetal growth. The fetal ß cells are stimulated to produce insulin,[2] an anabolic hormone which causes visceral enlargement and excess fat deposition,[7] resulting in the macrosomic infant. Higher rates of birth trauma and operative delivery are seen in these pregnancies,3, 8, 9 with resulting effects on maternal and neonatal morbidity.[2]

Fetal hyperinsulinaemia may also inhibit the pulmonary maturation processes necessary for surfactant production,[10] and so contribute to the increased incidence of respiratory distress syndrome seen in infants of diabetic mothers. The enhanced responsiveness of the fetal ß cell may extend into neonatal life and contribute to the development of neonatal hypoglycaemia.[10] Other indices of neonatal morbidity have been used as outcome measures. Maresh[11] found that

hypoglycaemia and polycythaemia, or admission to a special care baby unit was significantly related to the severity of gestational diabetes but not with maternal age or obesity. He also found that birth weight was more related to maternal obesity than to age or to severity of the gestational diabetes.

There are relatively few studies of fetal outcome in mothers with lesser degrees of hyperglycaemia in pregnancy. Talligaro[12] found an association with adverse fetal outcome – macrosomia, congenital abnormality, and delivery by caesarean section in mothers with milder degrees of hyperglycaemia in pregnancy. The Toronto trihospital study found a graded increase in adverse materno-fetal outcomes associated with increasing carbohydrate intolerance in women without gestational diabetes.[8] Roberts[6] did not find any adverse fetal outcome or neonatal morbidity, but he was able to demonstrate a significantly higher caesarean section rate for mothers with impaired glucose tolerance.

There is well established evidence that gestational diabetes increases the subsequent risk of developing diabetes mellitus.[2,3,13] The third International Workshop Conference on gestational diabetes[2] recommended that these women should be educated regarding symptoms of overt diabetes, and be followed up at regular intervals. There is evidence that the offspring of women with gestational diabetes have an increased risk of obesity in adolescence and of developing glucose intolerance in the future.[2] Identification and treatment of hyperglycaemia in pregnancy may thus have far reaching implications for the next generation.

There is no doubt that identification and treatment of mothers with frank diabetes in pregnancy is of benefit to mother and fetus. What is less certain is the benefit of identifying lesser degrees of hyperglycaemia, and screening for hyperglycaemia is the subject of much controversy. There is no consensus about who to screen, when to screen, which screening test to use, which diagnostic test to use, and how to interpret the results. The resulting effect is widespread variation in practice between different units, highlighted in two recent reports. Nelson-Piercy[14] looked at practices in one Regional Health Authority in London, and Jardine Brown[15] analysed a nationwide survey on screening for gestational diabetes. This latter report, compiled by the Pregnancy and Neonatal Care group, reveals that most units in the United Kingdom use routine testing for glycosuria and clinical risk factors as the basis for screening, with only a minority using routine blood glucose testing. The 75 g OGTT is the most widely used diagnostic test, being undertaken in many units solely because of positive clinical risk factors.

The aim of screening for a condition is to detect it at a stage where treatment will improve outcome. The screening test should be sensitive, specific, acceptable, and the treatment must be effective.[16] Jarrett[17] has argued that screening for gestational diabetes does not fulfil the criteria for a screening test; it does not have an agreed definition, and there is no consensus about management. He did however acknowledge the value of screening in predicting future risk of non insulin dependent diabetes for the mother, but found few, if any, benefits to the fetus. Carpenter [18] suggested that identification of pregnant women with previously unknown defects in carbohydrate metabolism 'may be justified as a screening measure for later diabetes, since women so identified may benefit from later medical follow-up'. He also referred to fetal benefits of diagnosis and treatment of hyperglycaemia in pregnancy in terms of reduced perinatal mortality and morbidity.

There are a number of screening tests in current use, with no consensus view as to the best method. Overall, the highest sensitivity and specificity for the outcome of a 100 g GTT is found with the 50 g oral glucose challenge test,[19] recommended by the American Diabetes Association.[20] In the UK, this method has not found favour,[15] and the methods used more commonly include:

(i) *Clinical risk factors (potential diabetic features)* such as glycosuria, previous infant >4.5 kg, previous stillbirth, neonatal death or congenital abnormality and maternal obesity. The use of these clinical risk factors alone has low sensitivity and specificity, 50% and 66% respectively in one review,[21] and 50 and 50% in another.[19] Coustan suggested that the taking of a history can be used as a screening test, and that the sensitivity can be increased by combining it with maternal age (>25 years) and obesity (pre-pregnancy weight >150 pounds), but screening by this method is thought to be relatively inefficient. Gillmer[22] in his review of diabetes in pregnancy found that at least 30% of patients with gestational diabetes do not have such features in their history.

(ii) *Glycosuria:* Sutherland [23] reported a prevalence of glycosuria in pregnant women of 11.3%, and found that glycosuria in a second fasting sample (not random glycosuria), was associated with an increased risk of gestational diabetes (15%). Pettitt[3] showed that random glycosuria in the third trimester was more common with increasing hyperglycaemia. However, a substantial number of women with hyperglycaemia in pregnancy will not have glycosuria, and as a screening method it is of low sensitivity.

(iii) *Random blood sugar* has been evaluated as a method of screening by various investigators. Jowett[24] and Nasratt[25] agreed that this method used alone was not an efficient screening test. O'Sullivan[13] however found that a random blood glucose, when combined with maternal age >25 years as a screening test, had a sensitivity of 88% and specificity of 82%. Maresht[21] in his review of glucose intolerance in pregnancy reported higher sensitivities when random blood glucose was combined with potential diabetic features as a screening test.

(iv) *Glycosylated haemoglobin (HbA_{Ic})* HbA_{Ic} is a useful indicator of blood glucose levels over the preceding 4-12 weeks. In diabetic pregnancy, high levels of HbA_{Ic} have been shown to be associated with an increased risk of congenital malformation[26] and perinatal death.[27] Although HbA_{Ic} is used by some units as a screening test for hyperglycaemia in pregnancy[15] its value has been questioned. It has been found to be of low sensitivity and specificity in one study[28] even though mean HbA_{Ic} levels were raised in patients with carbohydrate intolerance diagnosed by a 3 hr 100 g OGTT. In another study HbA_{Ic} was found to have a poor predictive value for pregnancy outcome. (Personal Communication) Lind recommended that all units use random blood glucose as a basis for screening, and the 75 g OGTT for diagnosis, interpreted by WHO criteria, for the sake of international uniformity in the diagnosis of hyperglycaemia in pregnancy.[29]

There is no consensus view as to the best method of screening for hyperglycaemia in pregnancy. In the absence of an agreed standard, Jardine Brown in the report of the pregnancy and neonatal care group[15] has suggested a screening protocol. This involves urine testing for glycosuria at every antenatal visit, timed random glucose measurements at booking, 28 weeks and if there is > + glycosuria). The report recommends that a 75 g oral GTT is performed, followed by a meal profile if the GTT is abnormal, before deciding on treatment.

Gestational diabetes, as defined by the WHO [30, 31] is diagnosed using a 75 g oral glucose tolerance test (OGTT) with blood glucose estimations at 0, 30, 60, 90 and 120 minutes, and defined cut-off points for diagnosis at 0 and 120 minutes. It now includes a category of "impaired gestational glucose tolerance" (IGT), an intermediate category between normality and gestational diabetes. In North America the 100 g OGTT is more commonly used for diagnosis of gestational diabetes, defined by the American Diabetes Association, using cut-off points at 0, 1, 2 and 3 hours (NDDG criteria).[2, 7] A 50 g OGTT is used by the Americans as a screening test to identify those mothers requiring a 100 g OGTT, but is used by some as the diagnostic test.[14]

The OGTT has traditionally been used to diagnose gestational diabetes. It uses an unphysiological glucose load [5] which may be unpalatable to pregnant women.[32] The results do not reflect the levels of blood glucose to which the fetus is normally exposed. It seems more logical, therefore, to study maternal glycaemic responses to the intake of normal foodstuffs, since it is hyperglycaemia in relation to normal diet that is likely to be associated with adverse fetal outcome.[33] Indeed, many centres measure blood glucose before and after a normal 'standardised meal, in mothers with an abnormal GTT result, before considering the need for treatment. We felt that it would be more logical to identify abnormal meal profile responses as the primary diagnostic process.[33] A number of studies have looked at maternal glucose responses to more physiological "meals". Sutherland and colleagues in Aberdeen[32] found that glucose response to a standardised breakfast test meal correlated more closely with percentile birth weight than the 75 g OGTT. Cheney and colleagues[34] showed different insulin and glucose responses to a breakfast tolerance test in lean and obese women with gestational diabetes.

They concluded that a simple breakfast meal test was useful in assessing pregnant women with gestational diabetes, and that it was more physiological than glucose loading. Roberts[5] compared the 75 g OGTT and a simple 300 kcal breakfast meal test for their ability to predict fetal outcome. He found that in the Belfast population,

neither test was a useful indicator of pregnancy outcome in mothers not already known to be diabetic, and that there was no benefit in continuing the test into the pre and post lunch period. Whether or not the breakfast test will be of any value in predicting the risk of future diabetes in the mother remains to be seen.

In conclusion, the breakfast meal test is as effective in detecting hyperglycaemia in pregnancy as the traditional 75 g OGTT. It is a more physiological test of glucose metabolism in pregnancy and is likely to be more acceptable to patients. We did not find any evidence of adverse fetal outcome associated with hyperglycaemia in pregnancy, but did find that there was a high incidence of subsequent Type 1 diabetes in those mothers found to have gestational diabetes. The forthcoming HAPO (Hyperglycaemia and Adverse Pregnancy Outcome) study aims to identify in a much larger population, made up of various ethnic groups in different countries, whether lesser degrees of hyperglycaemia in pregnancy are associated with increased risk of adverse maternal, fetal or neonatal outcome.

REFERENCES

1. Ritchie J W K. Diabetes and other endocrine diseases complicating pregnancy. In: Whitfield C R, editor. Dewhursts Textbook of Obstetrics and Gynaecology for Postgraduates. London: *Blackwell Science*; **1995**: 262-76.
2. Metzger B E. Summary and recommendations of the third international workshop conference on gestational diabetes mellitus. *Diabetes* 1991; **40**; suppl. 2: 197-201.
3. Pettitt D J, Knowler W C, Baird H R, Bennett P H. Gestational diabetes: Infant and maternal complications of pregnancy in relation to third trimester glucose tolerance in the Pima Indians. *Diabetes Care* 1980; **3**: 458-64.
4. Lind T, Phillips P R. A prospective multicentre study to determine the influence of pregnancy upon the 75 g oral glucose tolerance test (OGTT): The Diabetic Pregnancy Study group of the European Association for the study of Diabetes. In: Sutherland H W, Stowers J M, Pearson D W N, editors. Carbohydrate Metabolism in Pregnancy and the Newborn IV. London: *Springer-Verlag* 1989: 209-26.
5. Roberts R N, McManus J, Dobbs S, Hadden D R . A standardised breakfast tolerance test in pregnancy: comparison with the 75 g oral glucose tolerance test in unselected mothers and in those with impaired glucose tolerance. *Ulster Med J* 1997; **66**: 18-23.
6. Roberts R N, Moohan J M, Foo R L K, Harley J M G, Traub A I, Hadden D R . Fetal outcome in mothers with impaired glucose tolerance in pregnancy. *Diabetic Med* 1993; **10**: 438-43.
7. Dornhorst A, Chan S P. The elusive diagnosis of gestational diabetes. *Diabetic Med* 1998; **15**: 7-10.
8. Sermer M, Naylor C D, Gare D J, *et al.* Impact of increasing carbohydrate intolerance on maternal – fetal outcomes in 3637 women without gestational diabetes. *Am J Obstet Gynecol* 1995; **173**: 146-56.
9. Naylor C D, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance. Pathophysiology or practice style? *JAMA* 1996; **275**: 1165-70.
10. Skyler J S, O'Sullivan M J, Holsinger K K. The relationship between maternal glycemia and macrosomia. *Diabetes Care* 1980; **3**: 433-4.
11. Maresh M, Beard R W, Bray C S, Elkeles R S, Wadsworth J . Factors predisposing to and outcome of gestational diabetes. *Obstet Gynecol* 1989; **74**: 342-6.
12. Tallarigo L, Giampietro O, Penno G, Miccoli R, Gregori G, Navalesi R. Relation of glucose tolerance to complications of pregnancy in nondiabetic women. *N Engl J Med* 1986; **315**: 989-92.
13. O'Sullivan J B, Mahan C M, Boston A B. Criteria for the oral glucose tolerance test in pregnancy. *Diabetes* 1964; **13**: 278-85.
14. Nelson-Piercy C, Gale E A M. Do we know how to screen for gestational diabetes? Current practice in one regional health authority. *Diabetic Med* 1994; **11**: 493-8.
15. Jardine Brown C, Dawson A, Dodds R, et al. Report of the pregnancy and neonatal care group. *Diabetic Med* 1996; **13** Support 4: S43-S53.
16. Bates T. Screening for malignant disease. In: Kirk R M, Mansfield A, Cochrane J, editors. Clinical Surgery in General: RCS course manual. London: Churchill Livingstone 1993; 271-4.
17. Jarret R J. Gestational diabetes: a non-entity? *Br Med J* 1993; **306**: 37-8.
18. Carpenter M W, Coustan D R. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol* 1982; **144**: 768-73.
19. Coustan D R. Gestational diabetes. In: Reece E A, Coustan D R, editors. Diabetes Mellitus in Pregnancy: Principles and Practice. New York: Churchill Livingstone 1995: 703-13.
20. Ales K L, Santini D L . Should all pregnant women be screened for gestational glucose intolerance? *Lancet* 1989; **1**: 1187-91.
21. Maresh M J A. Glucose intolerance in pregnancy. (PACE review – No. 97/03) *Royal College of Obstetricians and Gynaecologists* 1997.
22. Gillmer M D. Diabetes in pregnancy. *Medicine International* 1983; **1**: 1639-40.

23. Sutherland H W, Stowers J M, McKenzie C. Simplifying the clinical problem of glycosuria in pregnancy. *Lancet* 1970; **I**: 1069-71.

24. Jowett N I, Samanta A K, Burden A C. Screening for diabetes in pregnancy: is a random blood glucose enough? *Diabetic Med* 1987; **4**: 160-3.

25. Nasrat A A, Johnstone F D, Hasan S A M. Is random plasma glucose an efficient screening test for abnormal glucose tolerance in pregnancy? *Br J Obstet Gynaecol* 1988; **95**: 855-60.

26. Ylinen K, Aula P, Stenman U-H, Kesäniemi-Kuokkanen T, Teramo K. Risk of minor and major fetal malformations in diabetics with high haemoglobin A1c values in early pregnancy. *Br Med J* 1984; **289**: 345-6.

27. Ylinen K, Raivio K, Teramo K. Haemoglobin AlC predicts the perinatal outcome in insulin-dependent diabetic pregnancies. *Br J Obstet Gynaecol* 1981; **88**: 961-7.

28. Cousins L, Dattel B J, Hollingsworth D R, Zettner A. Glycosylated haemoglobin as a screening test for carbohydrate intolerance in pregnancy. *Am J Obstet Gynecol* 1984; **150**: 455-60.

29. Lind T. Antenatal screening for diabetes mellitus. *Br J Obstet Gynaecol* 1984; **91**: 833-4.

30. World Health Organisation Expert Committee On Diabetes Mellitus. Second Report. Technical Report Series 646. *WHO Geneva* 1980.

31. World Health Organisation Study Group on Diabetes Mellitus. Technical Report Series 727. *WHO Geneva* 1985.

32. Sutherland H W, Pearson D W M, Lean M E J, Campbell D M. Breakfast tolerance test in pregnancy. In: Sutherland H W, Stowers J M, Pearson D W M, editors. Carbohydrate Metabolism in Pregnancy and the Newborn IV. London: *Springer-Verlag* 1989; 267-75.

33. Hadden D R. Hyperglycaemia in pregnancy – Screening methods for obstetric and internal medicine practice. *NUH-CME Review* 1992; **2**: 1-5.

34. Cheney C, Shragg P, Hollingsworth D. Demonstration of heterogeneity in gestational diabetes by a 400-kcal breakfast meal tolerance test. *Obstet Gynecol* 1985; **65**: 17-23.

The Ulster Medical Journal, Volume 69, No. 1, pp. 44-53, May 2000.

Fever hospitals in counties Armagh and Down : 1817-39

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Accepted 1 February 2000

SUMMARY

This paper outlines the provision for fever patients, (other than those suffering from cholera during the epidemic of 1832-34), in counties Armagh and Down in the two decades prior to the introduction of the Poor Law to Ireland. Possible causes of fever and the numbers of patients treated are discussed. The establishment and location of fever hospitals and the state of the premises are considered and an assessment of the contribution of these institutions to the development of medical provision in the early nineteenth century is also provided.

THE EPIDEMIC OF 1816-17

Fever was a frequent visitor to Ireland and one of the worst epidemics in the pre-Famine years occurred during the years 1816-19. According to one medical historian, it could:

> without fear of any charge of exaggeration be asserted that a more general epidemic never, perhaps, existed in any country of equal dimensions and population; for according to every account, whether public or private, it would appear that not only every city, town, and village was visited by the disease, but that even very few of the isolated cabins of the poor escaped.[1]

By the end of 1816 and during the early months of 1817 the contagion had become widespread. In Ulster, 'fever was uncommonly prevalent and destructive'.[2] There, it reached epidemic level quicker than in the other provinces. The epidemic spread more rapidly than elsewhere and declined at an equally quick rate. Indeed its duration in Ulster rarely exceeded a year and a half.[3]

In county Down, fever first appeared in October 1816 in the vicinity of Downpatrick. It became widespread the following spring and summer, reached its peak in 'prevalence and malignity' between July 1817 and March 1818 and from that time gradually subsided.

No class of society was completely exempt from attack. Mortality among the poor of county Down was cited as seldom exceeding 1 in 20, while it amounted to one in five among the more prosperous inhabitants However, when fever entered the houses of the poor, scarcely anyone escaped the infection. Unless there was a hospital in the vicinity, to which patients could be removed, the conditions in the homes of the poor demonstrated that it was impossible to separate the infected from healthy members of the family and to adopt the necessary measures of cleansing and ventilation. Among the poor, relapses were very frequent, particularly in the latter periods of the epidemic, and instances of recurrence of the disease were often observed: some individuals had it three times. Relapse was not so frequent among the wealthier classes where, in their families, a second individual contracting the disease was scarcely known.

Virtually every town, village and townland was affected, with the exception of Rostrevor which was described as a town 'out of the common thoroughfare, situated in a remarkably dry soil, with wide and airy streets, devoid of those miserable habitations where the lower orders of travellers and mendicants [were] lodged'.[5] During the summer months this town accommodated a considerable number of visitors who circulated 'a great deal of money among the inhabitants, who [were] thereby induced to keep their houses clean and in good order'.[6] In 1816, to alleviate the distress caused by scarcity of food, large contributions were made to the poor by the local

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gentry for the purchase of provisions, clothing and fuel. This too may have had some bearing on Rostrevor's fortunate escape from fever at this time. [7]

The neighbouring town of Newry, however, witnessed this 'very formidable epidemic' which began in 1816 and had increased alarmingly since March 1817.[8]

The fever was first observed in county Armagh in June 1817, when the towns of Armagh and Lurgan were affected. From that time until the following spring, the epidemic was most prevalent and fatal. At Armagh it was considered to have been the most destructive fever which had appeared for half a century and it was reported that in 1817 more people had died from it than during the preceding ten years. It proved most fatal to those who were advanced in life and those who were corpulent.[9] In Armagh city the mortality rate was high among many of the wealthier class who, due to their benevolent intentions may have come into contact with many of the stricken. Indeed the fever was deemed so severe that 'all those persons of the upper ranks who were attacked previous to September 28th, 1817, became its victims'.[10]

CAUSES AND RELIEF MEASURES

The causes which occasioned the spread of fever were similar in this part of Ulster to those elsewhere in the province and in the country generally. There was much unemployment and the people were scantily clothed. The cold and humidity of the seasons led to great scarcity and poor quality of provisions. Dr William Ryan wrote from Armagh in May 1818, that due to very high food prices, the distress was so great that many were obliged to use bran and pollard from the mills, boiled nettles and the refuse and stalks of kale to satisfy their hunger.[11] In county Down, the flour was so defective that 'peasants were frequently known to go a distance of thirty miles to procure bran or pollard, to enable them to make bread'.[12] The wet seasons in this period also caused turf shortages, which in many instances meant that food was eaten raw and clothes were hardly ever dry. Lack of ventilation in the dwellings of the poor was another factor which perpetuated the misery.

Vagrants and beggars were always regarded as being one of the ways by which the contagion was spread. Dr Atkinson of Armagh remarked that:

> the rainy season of 1816 and the great scarcity of provisions forced into towns, where they were assisted with fuel and provisions, many of the poor orders who often carried with them children ill of the confluent small-pox and measles and even of fever, for the purpose of exciting pity and obtaining relief, and these appear to have been the chief causes of disease, which was at first confined entirely to the poor.[13]

In Armagh during the winter of 1816-17 soup shops were established for the relief of the destitute. This encouraged the influx of

> an immense crowd of mendicants and poor of all descriptions into the town, who horded (sic) together in miserable lodging houses, lying on the floor on straw; and in many instances, taking up their quarters in the market house, or any place where they could procure shelter.[14]

The means adopted to prevent the spread of disease and their success were proportionate to the energy with which they were carried into effect. In the mountainous districts of county Down, where the inhabitants received no assistance or medical advice, the mortality was reported to have been excessive. In towns where neither fever hospital nor board of health was established scarcely a house escaped the contagion, while in others not more than one in four was visited by the fever. Early separation of the infected from the healthy; cleansing, whitewashing and ventilating the houses from which they were removed; and, as far as possible, the exclusion of mendicants were the usual measures adopted to contain the disease.[15] However, it was regrettable to note that the co-operation of the poor often met with almost insuperable difficulty. In some places, the personnel sent to cleanse the dwellings of the afflicted were refused admission and even maltreated; and the sick, though convinced of the contagious nature of the disease, were, at the beginning of the epidemic, most reluctant to be admitted to hospital. Such prejudice was almost completely overcome by the pressure of the evil, and the confidence of the poor in the benefit conferred on them by such establishments was soon widely acknowledged.[16]

THE OPENING OF FEVER HOSPITALS

A fever hospital was opened in Newry on 12th July 1817. Figures for this institution in Table 1 show that from its commencement until 18th February 1819, 1,494 patients were admitted. Admissions increased from 61 during the first two weeks of opening to a total of 116 in October

1817. In September, Dr Black reported that the applications for admission had been so numerous that it was necessary to procure a much larger house, and by the liberality of Lord Kilmorey the old custom-house was converted into a fever hospital. There was, ironically, a gradual decline from that time until March 1818 when numbers again rose steadily, reaching their peak of 150 cases the following July. From 1st to 18th February 1819, 13 patients were admitted – the fewest since the opening of the institution. During the 19 months, 41 died of fever and 16 of 17 fever-related diseases. The remainder were discharged cured.[17]

TABLE I

Monthly Report of the Fever Hospital in Newry, from its commencement 12th July 1817 to 18th February 1819 inclusive

Months Total	*Admitted*	*Died of Fever*	*Died of Disease Supervening Fever*	*Discharged Cured*	*Remaining*	*No. rec'g aid*
1817						
12-31 July	61	–	–	35	26	61
August	99	5	2	80	38	125
September	116	1	–	103	50	154
October	106	4	3	105	44	156
November	102	4	–	101	41	146
December	86	7	1	83	36	127
1818						
January	75	2	6	67	42	111
February	64	2	2	66	36	106
March	76	3	–	76	33	112
April	72	2	1	68	34	105
May	94	1	1	86	40	128
June	91	-	–	90	41	131
July	150	2	–	136	53	191
August	101	2	2	95	55	154
September	49	2	–	67	35	104
October	46	1	–	63	27	91
November	42	–	–	44	25	69
December	34	2	1	37	19	59
1819						
January	17	1	1	15	19	36
February 18	13	–	2	18	12	32
Totals	1,494	41	16	1,435	706	2,198

A fever hospital was opened in Armagh on 1st October 1817 and received patients until its closure in February 1818. The highest number of cases – 52 – was admitted during October 1817. Of these, three died and 21 were discharged cured. The following month 50 were admitted, seven died and 37 were discharged cured. In December the number of admissions had plummeted to 13; there was one death and 31 were cured. By January 1818, five patients were admitted and 19 discharged cured; there were no deaths. During the final month of the hospital's operation only one patient was admitted and was cured. This establishment reopened on 9th September 1818 when 42 patients were admitted and by the following month all these had been discharged cured. At this time the disease was much milder with the majority suffering from typhus miten.[18]

Apart from these two establishments there appears to be no evidence of any other fever hospitals in counties Armagh and Down during the 1816-19 epidemic. Fever hospitals of a more permanent nature were, however, erected several years later.

MORE PERMANENT INSTITUTIONS

At Newry, in 1825, when the dispensary was established, a fever hospital was founded on the same site. Their aim was to 'relieve the sick and to provide comfort to fever patients'.[19] The population of the district attached to this institution amounted to almost 18,000. It was supported by Grand Jury Presentments[20] and by private contributions and managed by a committee who appeared to discharge their duties conscientiously. In addition to the surgeon, there was one attendant resident in the hospital who acted as matron, nurse and cook. The building had originally been a corn store. The upper storey was divided into two wards which could accommodate eight beds. Each ward was provided with a fireplace and was well ventilated, but access was by a wooden staircase constructed on the outside of the building. Bedsteads for patients were of iron, and ample supplies of bedding consisted of straw mattresses, which were destroyed when each patient was discharged, some loose straw, sheets, blankets and rugs. Facilities for washing and sanitation were, however, non-existent as there was 'no wash-house or scullery, or other out-offices, nor any yard or garden'.[21]

Unfortunately, most figures for this establishment do not differentiate between patients treated in the fever hospital and those relieved at the dispensary. However, several reports give some indication of the efficacy of the fever hospital in the treatment of sufferers. In January 1827, seven patients remained in the hospital from the previous month, and 107 were admitted during the year. Of these, 99 were discharged cured and seven died. This achievement was regarded by the chairman of the management committee as 'peculiarly valuable in a year more than usually marked by the prevalence of contagious fever'.[22] In course of the year 1831 there was a total of 198 patients, 186 of whom were discharged cured. There were two deaths from fever and two from consumption and smallpox. In his report for that year the surgeon at Newry commented on the importance of the institution's work:

> The Fever Hospital is of incalculable benefit to the community; it is an asylum for those sick poor, whose disease, if unrestrained must expose a large circle of the public to imminent danger, and by this means it contributes exceedingly to check the extension of fever in this town and neighbourhood.[23]

In 1832, the number of fever cases amounted to 211, a figure which fell to 118 the following year.[24] Fever was not so prevalent in 1834 and indeed must not have been as serious. Only 86 patients were admitted during that year, yet an additional 207 cases were treated out of hospital. There was a total of 12 deaths – three intern patients and nine extern.[25] Larger numbers were recorded in 1840, most of whom lived in fairly close proximity to the institution. In that year, 360 patients were admitted, the majority of whom – 325 – lived within five miles of the town; 30 resided from five to ten miles away, and five more than ten miles distant. There were 18 deaths in 1840, indicating a mortality rate of five per cent.[26]

Conditions for admission were similar to those imposed generally on applicants for relief, namely the possession of a subscriber's ticket. Patients were not required to engage in labour during their stay in hospital. They were, nevertheless, subject to certain regulations designed to ensure good conduct and they were permitted to have visitors on five days each week.[27] Reports from the Newry establishment indicate that patients other than those suffering from fever were treated there. In 1835, for example, it was reported that the number of scalds, burns, wounds, fractures, dislocations and contusions was proportionately large, and several of the worst were admitted to hospital. In

addition, there were three amputations of the leg, all performed in the hospital.[28]

In 1830, when a new county infirmary was planned for Downpatrick, the governors decided to erect a fever hospital on the same site. This was organised and financed in a similar way to the infirmary: by private subscriptions and Grand Jury Presentments. A board of governors separate from that of the infirmary was elected in June 1833[29] and the first patients were admitted on 31st January 1834. The importance of the charity was attested by the steady rise in annual contributions. The first year's subscriptions, collected in 1833, totalled £71 8s. This amount increased in 1834 to £96 14s and to £133 6s 6d in 1835.[30]

The two-storey stone building contained eight wards with a total of 40 beds. Sewerage was good and there were baths and toilets. The hospital received patients suffering from 'all diseases likely to become epidemic and occurring in any part of the county'.[31] It would evidently prove beneficial as the neighbouring county infirmary afforded no assistance in these circumstances.

Three medical attendants were connected to the hospital, one of whom was also attached to the infirmary. The other two doctors lived in Downpatrick and were engaged in private practice.

According to the Assistant Commissioners inquiring into the state of the poor, they carried out their duties most conscientiously and efficiently. Each physician had a male and female ward under his separate charge. Daily visits were made and the resident apothecary was always at hand to assist in cases of emergency and to dispense the necessary medicines.[32] The three physicians, who were appointed by annual subscribers of one guinea or more, gave their services to the charity without remuneration – a fact commented on favourably by the Assistant Commissioners:

> It must be confessed that it is rather a curious circumstance to see the dangerous duties of a fever hospital quite as well performed *gratis*, as those of a county infirmary close by for a handsome salary and a most splendid house.[33]

The apothecary, however, received a salary of £20 per annum and other members of staff were paid as follows: matron: £12 per annum; cook (who was also first nurse): £6; second nurse £6; and porter £8 8s.[34]

All fever sufferers were entitled to immediate admission, unconditionally. No extern patients were attended, but there was an arrangement by which any person – rich or poor – could be received into the hospital on an advance payment of £1, with a further 5s per week to be paid for the duration of the stay. No uniform diet was formulated, but each physician regulated the type and quantity of food required by individual patients. Clothing was not supplied by the hospital, nor was there any provision for cleansing and purifying the clothes which patients brought with them. Unfortunately, such short-sightedness, in some instances proved fatal.

The dangers of contracting fever by employees of the establishment and by those in close contact with sufferers were continually present. In November 1836, 'a fever of a particularly malignant type prevailed in the hospital'.[35] This had been introduced by a 'wandering beggar' from county Louth and he was the first to fall victim to it. It was later ascertained that eight families who, in the course of a few days had given him shelter in their homes, were attacked and three individuals died. At the hospital the nurse and the porter each contracted this fever which, in a short time led to their deaths.[36]

The members of the hospital committee were eager to emphasise that the institution provided treatment for the poor of the whole county. This was reflected in the distinction made in admission figures between those patients who were inhabitants of Downpatrick and those who resided outside the town. In 1834, the number of patients admitted to the hospital was 63, 53 of whom came from the surrounding country and ten from the town. In the following year, 77 patients were admitted, 59 of whom came from outside the town and 18 lived in Downpatrick itself.[37] During 1836, 95 patients were admitted to the hospital. The committee members were delighted that 73 out of those 95 cases had come from 'the country districts' and were eager to publicise the utility of the institution even more extensively, so that more patients from distant parts would avail themselves of its benefits. They wished to impress upon the rural population the importance of sending patients to the hospital as early as possible. This was evidently to increase the prospects of recovery and to remove the sufferers from the close contact which pertained within the family unit. To assist in transporting patients to the

hospital, the committee kept a 'covered fever cart' which could be provided on application.[38]

In 1837 typhus was prevalent in Downpatrick and the surrounding area. This, together with the increasing confidence in the fever hospital and the diminution of those prejudices which initially rendered so many unwilling to send their relatives as patients to the establishment, may account for the rise in admissions during that year.[39]

During 1840, as in Newry, the number of patients admitted reached the 'unusually large' figure of 327. Of these, 166 resided in Downpatrick itself, 138 lived between five and ten miles from the hospital and 23 more than ten miles distant. A comparison with the admission figures for the Newry establishment show that, in that same year – 1840 – at Downpatrick the numbers of patients admitted to the fever hospital from more than five miles away (161), was almost equal to the numbers of those who resided within a five mile radius of the institution (166). At Newry, only 11 per cent of patients resided more than five miles away.[40] The members of committee would obviously have been pleased that such a trend as intimated in their 1836 report had continued. However, the Assistant Commissioners in their 1841 report on *Medical Charities* quote figures supplied by the resident apothecary at Downpatrick, which suggest that out of 105 admissions in an unspecified year, 85 resided within five miles of the town, 17 lived between five and eight miles from the hospital and three came from a distance of more than eight miles.[41] They concluded that fever hospital relief was therefore 'only partially supplied to the sick poor of this Union'.[42]

ADDITIONAL ACCOMMODATION

In addition to the two county fever hospitals, there was some limited provision for sufferers at Hillsborough. Here, on the dispensary premises, were located three wards which could provide accommodation for ten patients. Although the wards were described as being 'low and confined' they were, nevertheless, 'considered adequate to the wants of the poor accruing from serious accidents or bad cases of fever'.[43] The Hillsborough establishment does not appear to have been used consistently nor indeed solely for the treatment of fever patients. In 1835, the Assistant Commissioners reported that there were no intern patients but that the rooms were still furnished. The dispensary report for 1836 stated that the hospital which was 'appropriated for accidents and non-contagious diseases' had proved 'a useful appendage to the institution as it afforded accommodation to several who could not be properly attended to in their own homes'. Furthermore, it was suggested that measures were in progress for the establishment of a hospital 'in the neighbourhood of the town for fever patients'.[44] Such an institution was indeed founded, and in 1840 admitted 82 patients.[45] Admission to the fever hospital was evidently not free as the medical superintendent's 1841 report indicated:

> Patients were received into the fever hospital, which comprises four wards, containing nine beds, on the payment of five shillings being made for each. Those who could afford it, from a sense of the value of the institution, have willingly contributed ten shillings, and, in some instances, a pound, for admission.[46]

About this time a subscription list was opened with a view to extending the fever hospital, but it was decided to postpone any further action on this pending the outcome of possible legislation.[47] The foundation stone of a new building was eventually laid on 26th July 1844. The cost was apparently to be met by the Marquis of Downshire,[48] who, according to a later report, presented 'the new fever hospital erected by him at Hillsborough at a cost of upwards of £1,200, independent of the site and value of grounds attached, besides a most liberal annual subscription, to the Corporation, constituted by the act of 58th Geo, III, chap. 47, for establishing fever hospitals'.[49]

At Armagh, a fever hospital, supported solely by the munificence of his Grace the Lord Primate, was opened in 1827. This 'chaste and handsome building of hewn limestone' cost approximately £3,000 which was defrayed by the Primate. The accommodation included wards for male and female patients on the first and second floors respectively. Each floor contained two wards – a fever ward and a recovery ward, the former having ten beds and the latter five, making a total of 30. The hospital received praise for its standard of cleanliness, its economy, and its 'suitable accommodation for its suffering inmates' and ranked 'among the first in the province'.[50] This institution was also considered 'remarkable' by the Assistant Commissioners who commented on the 'excellent economy of its administration' and 'the important sanitary results which it has produced'.[51] Numbers of patients relieved or

admitted fluctuated depending on the prevalence of fever as the figures below indicate:

TABLE II

Patients relieved/admitted to Armagh Fever Hospital 1827-33[52]

Relieved	*1827*	*1828*	*1829*	
	38	100	58	
Admitted	*1830*	*1831*	*1832*	*1833*
	15	183	147	134

Staff at this hospital were, like those in other institutions, continually in danger of contracting fever. Within the first seven years of opening, the matron had two attacks of typhus; her daughter had one attack and a nurse also suffered.[53]

In 1840, the Armagh hospital contained 40 beds, intended for those fever sufferers who lived within the borough. At most dispensary meetings the subscribers expressed a desire that provision should be made for supplying fever hospital relief to the class of poor who were 'not destitute in health', but whose means could not afford 'the necessary aid or the necessary convenience, in time of severe illness'. [54]

A fever hospital was established at Middletown, county Armagh, in 1832, by the trustees of the charities of the late Bishop Sterne.[55] A dispensary, opened in February 1834, was housed in the same building. The hospital provided accommodation for 16 patients, although for several months after it opened no fever cases were admitted. During the local cholera epidemic of 1833, 81 individuals contracted the disease. Of these, 35 cases proved fatal and 46 were cured.[56] The charity housed and treated 40 patients at this time and was, undoubtedly, considered most beneficial to the parish.[57]

This establishment derived no assistance whatever from the county, nor from any source other than the bequest cited earlier. Neither did the trustees contemplate applying for a county grant, as the funds at their disposal amounted to £1,800 per annum and clearly appeared sufficient. The concept of such a charity received commendation from the Assistant Commissioners, who considered it 'a most judiciously managed example of what may be done in this country for a given sum, in the way of small, local hospital accommodation . . .'.[58] They were, nevertheless, disappointed that reception and treatment of patients was restricted to those suffering from 'two diseases of rare occurrence'.[59] Further evidence suggests that this institution was used as an infirmary, but as no division of cases admitted could be obtained, it remained enumerated among the fever hospitals.[60]

The third fever hospital in county Armagh was situated at Tandragee and was exclusively for the benefit of fever patients who lived in that dispensary district. It had been built originally as a cholera hospital, but was later converted into a fever hospital, financed by donations and the contributions from a charity sermon, and supervised by the medical attendant of the dispensary. It was described as 'a good commodious building . . . divided into two wards . . . furnished with nine iron bedsteads, straw mattresses and a good supply of bedclothes'.[61] According to the medical attendant, during the winter of 1832, there were 40 in-patients at one time. Two years later this figure had plummeted to two.[62] In 1839, 42 patients were admitted. At that time it appeared to be 'well-managed' and was considered 'to be very useful, both for the prevention and cure of disease'.[63]

In the early 1830s, the inhabitants of Keady were concerned that the county hospital at Armagh was of little or no benefit to the poor in their area, and indeed that the fines levied at the Keady Petty Sessions, were, by an Act of parliament, appropriated by the Armagh infirmary.

Therefore, a small hospital attached to the dispensary was opened. Initially, it appears to have received patients other than those suffering from 'cholera and fevers'.[64]

However, later evidence shows that as circumstances in the county deteriorated it was used, perhaps solely, as a fever hospital. Very few patients were treated in the early 1840s: five in each of the years 1841, 1842, 1844 and 1845; seven in 1843; and six in 1846. By 1847, when 410 cases were received, this establishment had, like many others in Ireland, definitely assumed the function of a fever hospital. This was, however, short-lived, for by the first quarter of 1851 only one patient was treated.[65]

ASSESSMENT

In 1841, there were 91 fever hospitals in Ireland.[66] Between the years 1831 and 1841, 243,427

individuals were received at these institutions and 15,988 deaths were recorded – a ratio of mortality to receptions of 1 in 15.24. In the Ulster counties, the number of receptions for that period totalled 10,974, and 907 of these – a ratio of 1 to 12.1 – died. The hospitals in county Armagh (Armagh and Middletown) which are cited in the statistics for these years, record 2,412 patients received and 143 deaths, giving a ratio of mortality to reception of 1 to 16.87. In county Down, only the figures for the Downpatrick establishment are quoted. These show that of the 1,206 patients received, 102 died – a ratio of 1 to 11.82. It is difficult to draw any definite conclusions from these figures regarding the standard and efficacy of treatment and care, since there are several variables to be considered – for example the figures do not categorise the seriousness of the cases received at the institutions, nor do they show the height the fever had reached on referral to the hospitals. Furthermore, the figures are limited to very few hospitals and other institutions for the treatment of fever in these counties are not recorded.

Generally, however, the removal of cases to hospital must have been the means of preventing an equal number, perhaps many more, from being stricken with fever, and consequently, of saving the lives of at least as many as died in the institutions. The support of patients in hospital preserved a considerable number of families from becoming paupers. It was noted that when fever attacked two or three members of a poor family, pauperism and mendicity were consequential, as the members of the family were obliged to pawn or dispose of their clothes and any little furniture they possessed, in order to obtain food and drink for those suffering from the illness at home. There was also an advantage for the medical profession in having these hospitals established, as doctors had consistent opportunities to acquaint themselves with the nature and treatment of fever, and were, therefore, able to monitor the various stages of the epidemic and to employ the relevant treatment for each.

As with infirmaries and dispensaries, these hospitals were dependent on subscriptions; thus, failure of the wealthy to contribute towards them signified that many towns and districts were restricted from much possibility of access to them. Even in counties Armagh and Down, many areas were so remote from the few hospitals, that treatment of fever patients was completely impossible. In areas where small fever hospitals were established, these appeared not to be fairly distributed in proportion to the population, and in general, their benefits were intended for a small surrounding district. Some of the larger fever hospitals in towns were also less beneficial than might have been expected, as relief was confined to a comparatively small area, although in Newry, the one mile radius surrounding the fever hospital included a population of approximately 18,000. Considering the prevalence of fever, it is surprising that, even in counties Armagh and Down, where landlords and local gentry were quite actively involved in charity work, so few of these institutions were established. It is possible that the erratic nature of fever outbreaks may have caused the planning of certain temporary fever hospitals, but, if the fever subsided within a short period, such plans were abandoned.

In 1839, the fever hospitals in county Armagh served a population of 220,134 and those in county Down 352,012 – probably most inadequate for the needs of a rising population. However, this would be addressed through the implementation of Poor Law legislation in Ireland and the establishment of the workhouse fever hospitals which would, of course, assume a pivotal role in the treatment of patients in the immediate future.

REFERENCES

1. Harty, W. *An Historic Sketch of the Causes, Progress, Extent and Mortality of the Contagious Fever epidemic in Ireland during the Years 1817, 1818, and 1819.* Dublin: 1820, p.110.
2. Barker, F & Cheyne, J. *An Account of the Rise, Progress and Decline of the Fever lately epidemical in Ireland, Vol. 1.* Dublin: Hodges & McArthur, 1821, p.460.
3. O'Neill, T P. Fever and Public Health in pre-famine Ireland, in *Journal of the Royal Society of Antiquaries of Ireland* 1973; **103**: 9.
4. *Appendix to First Report from the Select Committee on the State of Disease and Condition of the Labouring Poor in Ireland,* H C 1819 (314) viii, 3. (hereafter, *Appendix to First Report from the Select Committee,* 1819).
5. *Ibid.*
6. *Ibid.*
7. *Ibid.*
8. Barker & Cheyne, *op.cit.,* p.35.
9. Dr Atkinson, in Barker & Cheyne, *op.cit.,* p.466.
10. Dr William Ryan, in Barker & Cheyne, *op.cit.,* p.467.

11. Barker & Cheyne, *op.cit.*, p.346.
12. *Appendix to First Report from the Select Committee,* 1819.
13. Barker & Cheyne, *op.cit.*, p.462.
14. *Appendix to First Report from the Select Committee,* 1819.
15. *Ibid.*
16. *Ibid.*
17. *Ibid.*
18. *Ibid.*
19. Day A & McWilliams P (eds). *Ordnance Survey Memoirs Parishes of County Down I, 1834-6, South Down,* (Belfast: The Institute of Irish Studies, The Queen's University of Belfast, 1990), p.80.
20. 58 George III, c.47.
21. *First Report from Commissioners for inquiring into the state of the Poor in Ireland with Appendices and Supplement.* Appendix B. 1835 (369) xxxii Part II (hereafter *Poor Inquiry*).
22. Newry Dispensary and Fever Hospital Third Report, *Newry Commercial Telegraph*, 5 February 1828.
23. Newry Dispensary and Fever Hospital Seventh Report, *Newry Commercial Telegraph*, 10 February 1832.
24. *Poor Inquiry*, Appendix B.
25. Medical Report of the Newry Dispensary and Fever Hospital for the year 1834, *Newry Commercial Telegraph*, 20 January 1835.
26. *Report of the Poor Law Commissioners on Medical Charities, Ireland with Appendices.* 1842 (324) xi (hereafter *Medical Charities Report*, 1841), Appendix A, No. 3.
27. *Poor Inquiry*, Appendix B.
28. Medical Report of the Newry Dispensary and Fever Hospital for the year 1835, *Newry Examiner*, 30 January 1835.
29. *Down Minutes*, 17 June 1833, (PRONI, HOS 14/2/1).
30. Day A and McWllllams P (eds). *Ordnance Survey Memoirs, Parishes of County Down IV, 1833-7, East Down and Lecale,* Belfast: The Institute of Irish Studies, The Queen's University of Belfast, 1990) p.46.
31. *Poor Inquiry*, Appendix B.
32. *Ibid.*
33. *Ibid.*
34 *Ibid.*
35. Annual Report of the Committee of the Downpatrick Fever Hospital, 1836, in *Minute Book of Board of Governors of Downpatrick Fever Hospital*, (PRONI, HOS 14/2/2).
36. *Ibid.*
37. Day A and McWilliams P (eds). *Ordnance Survey Memoirs, Parishes of County Down IV, 1833-7, East Down and Lecale,* p.46.
38. *Downpatrick Fever Hospital Minutes*, January 1836, (PRONI, HOS 14/2/2).
39. The report of the committee for 1837 does not quote specific figures for admissions.
40. *Medical Charities Report*, 1841, Appendix A, No. 2.
41. *Medical Charities Report*, 1841, Appendix B, No. 6. This brief report pertains to Downpatrick Poor Law Union and although not stated, the total number of admissions may refer only to those patients residing within that union.
42. *Ibid.*
43. *Poor Inquiry* Appendix B.
44. Hillsborough Dispensary Report in Day A and McWilliams P (eds). *Ordnance Survey Memoirs, Parishes of County Down III, 1833-7, South Down,* (Belfast: The Institute of Irish Studies, The Queen's University of Belfast, 1990), p.96.
45. *Medical Charities Report*, 1841, Appendix A, No. 3.
46. Hillsborough Dispensary Report for the year ending 31 December 1841, *Dublin Medical Press* 1842; **7**: 137.
47. *Medical Charities Report*, 1841, Appendix B, No. 6.
48. *Banner of Ulster*, 30 July 1844.
49. *Ibid.*, 10 March 1846. A dispute arose between the Marquis and the Board over the appointment of a medical officer, and at the beginning of 1847 the Marquis announced that, in future, he would undertake the support of the institution himself. Medical aid was, therefore, for a time, confined to the Downshire tenantry. See Barry J. *Hillsborough, A Parish in the Ulster Plantation*, Belfast: Wm. Mullan & Sons Ltd., 1962, p. 29.
50. Lewis S. *A Topographical Dictionary of Ireland Vol.1.* London: S Lewis & Company, 1837, p.74.
51. *Poor Inquiry*, Appendix B.
52. Figures for the years 1827-30 quoted as the number 'relieved' in H C 1830 (667), vii; those 'admitted' for the years 1831-33 quoted in *Poor Inquiry*, Appendix B.
53. *Poor Inquiry*, Appendix B.
54. *Medical Charities Report*, 1841.
55. Dr Sterne was former Bishop of Clogher who, in his will dated 13 May 1741, bequeathed to the village of Middletown certain lands in counties Armagh and Monaghan. Money from these lands was to be used for charitable purposes.
56. Day A and McWilliams P (eds). *Ordnance Survey Memoirs, Parishes of County Armagh, 1835-8, Vol. 1.* Belfast: The Institute of Irish Studies, The Queen's University of Belfast, 1990, p. 129.
57. *Poor Inquiry,* Appendix B.
58. *Ibid.*

59. *Ibid.*
60. *Census of Ireland*, 1851, H C 1856 (2087 I), xxix.
61. *Poor Inquiry*, Appendix B.
62. *Ibid.*
63. *Medical Charities Report*, 1841.
64. *Poor Inquiry*, Appendix B.
65. *Census of Ireland, 1851, Reports of Commissioners,* H C 1856 (2087 I), xxix.
66. *Ibid.*

The Ulster Medical Journal, Volume 69, No. 1, pp. 54-57, May 2000.

Case Report

Life-threatening laryngeal oedema in a pregnant woman with hereditary angioedema

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Accepted 8 December 1999

Hereditary angioedema is an unusual condition that has been associated with a high mortality rate during acute attacks. The disease is felt to have a benign course in pregnancy, but some reports indicate a worsening of attacks in pregnant women. A case of a pregnant woman with known hereditary angioedema presenting with life-threatening laryngeal oedema is reported, and is followed by a discussion of the disease, its links with sex hormones and a review of the literature.

CASE REPORT A 26-year-old primigravidum woman, pregnant at 25 weeks gestation, was admitted with a two-hour history of a sensation of swelling in her neck. She and her sister had been diagnosed as having type I hereditary angioedema four years previously through family screening following the discovery of a similar diagnosis in her mother. This diagnosis was made on the basis of serum analysis revealing decreased levels of C1 inhibitor (<0.04 g/1; normal range 0.28-0.50 g/l), functional C1 inhibitor (7% of normal levels) and C4, the fourth component of complement (<0.06 g/1; normal range 0.2-0.5 g/1) and normal levels of C3, the third component of complement (1.03 g/1; normal range 0.5-1.2 g/l). Her health prior to her pregnancy had been good with only three short-lived episodes of angioedema affecting her hands alone and one episode of facial swelling following a dental procedure. Since becoming pregnant, there had been an increase in the frequency and duration of the angioedematous episodes, with swelling in her arms, legs and shoulder occurring, on average, once per week.

She was not dyspnoeic and had no foot or arm swelling; her sole complaint was the swelling sensation in her neck which was giving rise to some difficulty in swallowing. On examination she appeared comfortable; her temperature was 36.2° C, with a heart rate of 96 beats per minute, blood pressure of 108/58 mmHg and oxygen saturations of 98% on room air. Cardiovascular and respiratory examinations were normal and abdominal examination was consistent with pregnancy of 25 weeks gestation. There was no evidence of swelling in her throat, neck or peripheries.

She was treated with 200 mg of hydrocortisone and 10 mg of chlorpheniramine intravenously and admitted for observation.

Three hours later she felt that her breathing had become more difficult. Examination of her oropharynx revealed swelling of the soft palate with the vocal cords moving and the airway intact. Observations and clinical examination otherwise were still normal.

A further three hours later she developed respiratory distress with stridor. Examination revealed pharyngeal swelling with the vocal cords viewed only with difficulty. She received one unit of fresh frozen plasma with some improvement of her symptoms and signs and was then given 2000 units of C1 inhibitor concentrate, which led to complete resolution within 30 minutes.

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She had no further problems while in hospital and was discharged five days later on tranexamic acid. The rest of the pregnancy was uneventful. The delivery was vaginal and uncomplicated with prophylactic administration of C1 inhibitor concentrate 1000 units on the day of delivery and the following two days. A healthy male infant was born. To date he has not been screened for hereditary angioedema.

DISCUSSION

Hereditary angioedema (HAE) is an unusual condition characterised by recurrent episodes of localised, well-circumscribed, non-pitting oedema. It may affect any part of the body, but more commonly involves the extremities, trunk, face, throat and the abdominal viscera where it causes pain. Involvement of the larynx is particularly dangerous, with a high mortality rate.[1,2] More recent clinical observations include symptoms of urinary tract infection in women, an increase in spontaneous abortions and premature labour, and more frequently reported heartburn and rheumatic complaints.[3]

The hereditary nature of the disease was first described by Osler in 1888,[4] and it is transmitted in a Mendelian autosomal dominant manner.[5] Investigation of the biochemical abnormality underlying HAE began with the identification and characterisation of C1-inhibitor.[6] C1-inhibitor is an $\alpha 2$ globulin that blocks the esterolytic activity of the first component of the classical component pathway.[7] It also has inhibitory actions on the fibrinolytic and kallikrein-kinin systems.[8] Subsequently a deficiency of this serum protein in individuals with HAE was discovered.[9] There are two forms of HAE, type I in which there is both absent or decreased C1-inhibitor antigenic levels and decreased functional activity, and type II, in which a dysfunctional protein is produced leading to normal C1-inhibitor antigenic levels but markedly reduced functional activity.[10] Both forms have decreased levels of the fourth component of complement. In acute attacks of HAE, the deficiency of C1-inhibitor allows unrestricted activation of the complement, fibrinolytic and kallikrein-kinin systems with increased generation of plasmin[11] and bradykinin[12] which causes localised oedema through enhanced vascular permeability and extravasation of fluid.[13]

The C1 inhibitor gene is located on chromosome 11 (p.11.2-q-13), where mutations in the structural gene region are responsible for HAE.[14] A particular region of the gene contains direct repeats of the triplet CAA, making it susceptible to mutation.[15] There is considerable genetic heterogeneity in the disease, with a number of mutations described.[16-20]

The initial presentation of HAE is typically early in life, with over 50% having their first attack in the first decade of life.[8,21,22] It affects a wide diversity of ethnic groups.[21] The most common precipitants of an acute attack are trauma, emotion,[1] insect stings and food.[2]

HAE appears to follow a benign course in pregnancy.[8,21] However, case reports have described an increase in the incidence and severity of attacks,[23-25] while labial oedema caused by vaginal delivery has been the first clinical presentation of the disease.[26] Indeed, vaginal delivery leading to perineal oedema and hypovolaemia has caused maternal mortality.[27] Caution is advised in making a diagnosis of HAE in pregnancy, as levels of C1 inhibitor may be decreased in normal pregnant women, returning to normal levels after delivery.[28]

The role of oestrogen in HAE has been debated. An increase in attacks has been reported during menstruation,[8,22] with oral contraceptives causing greater frequency and severity of attacks.[2,8,29] The mean values of both C1 inhibitor activity and antigen titres are significantly decreased in normal women using oral contraceptives compared to non-users.[29] Familial, oestrogen-linked angioedema attacks not caused by C1 inhibitor deficiency have also been described.[30]

The treatment of HAE has been traditionally divided into three groups i.e. treatment of acute attacks, long-term prophylaxis and short-term prophylaxis. Attempted therapy with adrenaline, antihistaminic agents or corticosteroids has no role or benefit in patients with HAE.[8] The mainstay of the treatment of acute episodes of HAE is replacement therapy, successfully used in the therapy of other serum protein deficiencies such as haemophilia and hypogammaglobulinaemia. Infusion of fresh frozen plasma has been shown to be beneficial,[31] although concerns exist that it may theoretically worsen the attack.[32] C1 inhibitor concentrate has also been shown to be safe and effective in the resolution of acute episodes.[33] Given in doses of 500 to 1000 units intravenously, oedema begins to resolve within 30 minutes to two hours of injection, with complete remission within 24 hours.[32]

Agents effective in long-term prophylaxis include attenuated androgens and antifibrinolytics. The main androgen used is danazol, which has been shown to decrease the severity and frequency of attacks, with biochemical assays of C1 inhibitor and C4 returning to normal levels.[34-36] The doses used should be the minimum needed to control attacks, as significant dose-related adverse reactions have been reported, including weight gain, myalgia, headaches, microscopic haematuria, altered liver function tests, anxiety, altered libido, alopecia, dizziness and nausea.[38, 39] Danazol also has virilizing effects on a female foetus if used in pregnancy.[37] Stanozolol is another androgen with a similar efficacy and side effect profile.[40] Two antifibrinolytic agents, ε-aminocaproic acid and transexamic acid are reported to assist in the control of HAE, but have a number of serious side effects including muscle necrosis and a potential thrombotic tendency.[41, 42] Fresh frozen plasma has also been used for long-term prophylaxis in a pregnant woman with HAE.[43]

Short-term prophylaxis is important in individuals with known HAE who are undergoing procedures which can potentially precipitate an attack, including surgery, dental work or labour. Attenuated androgens may be used in pregnancy,[44] but there is the potential risk of virilization of a female foetus, and this risk has been cited, at least in part, as an indication for termination of pregnancy in a woman with HAE.[45] Fresh frozen plasma[46] and C1 inhibitor concentrate[22, 47] have both been advocated for short-term prophylaxis in these situations.

REFERENCES

1. Dennehy J J. Hereditary angioneurotic oedema. Report of a large kindred with defect in C'1 esterase inhibitor and review of the literature. *Ann Int Med* 1970; **73**: 55-9.
2. Winnewisser J, Rossi M, Spath P, Burgi H. Type I hereditary angio-oedema. Variability of clinical presentation and course within two large kindreds. *J Int Med* 1997; **241**: 39-46.
3. Nielsen E W, Gran J T, Straume B, Mellbye O J, Johansen H T, Mollnes T E. Hereditary angio-oedema: new clinical observations and autoimmune screening, complement and kallikrein-kinin analyses. *J Int Med* 1996; **239**: 119-30.
4. Osler W. Hereditary angio-neurotic edema. *Am J Med Sci* 1888; **95**: 362-7.
5. Crowder J R, Crowder T R. Five generations of angioneurotic edema. *Arch Intern Med* 1917; **20**: 840-52.
6. Pensky J, Levy L R, Lepow I H. Partial purification of a serum inhibitor of C'1-esterase. *J Biol Chem* 1961; **236**: 1674-9.
7. Colten H R. Hereditary angioneurotic edema 1887-1987. *New Engl J Med* 1987; **317**: 43-5.
8. Frank M M, Gelfand J A, Atkinson J P. Hereditary angioedema: the clinical syndrome and its management. *Ann Int Med* 1976; **84**: 580-93.
9. Donaldson V H, Evans R R. A biochemical abnormality in hereditary angioneurotic edema. *Am J Med* 1963; 35: 37-44.
10. Rosen F S, Charache P, Pensky J, Donaldson V H. Hereditary angioneurotic edema: two genetic variants. *Science* 1965; **148**: 957-8.
11. Cugno M, Hack C E, DeBoer J P, Eerenberg A J M, Agostoni A, Cicardi M. Generation of plasmin during acute attacks of hereditary angioedema. *J Lab Clin Med* 1993:**121**: 38-43.
12. Nussberger J, Cugno M, Amstutz C, Cicardi M, Pellacani A, Agostoni A. Plasma bradykinin in angio-oedema. *Lancet* 1998; **351**: 1693-97.
13. Shoemaker L R, Shurman S J, Donaldson V H, Davies III A E. Hereditary angioneurotic oedema: characterization of plasma kinin and vascular permeability-enhancing activities. *Clin Exp Immunol* 1994; **95**: 22-8.
14. Stoppa-Lyonnet D, Tosi M, Laurent J, Sobel A, Lagrue G, Meo T. Altered C1 inhibitor genes in type I hereditary angioedema. *New Engl J Med* 1987; **317**: 1-6.
15. Bissler J J, Cicardi M, Donaldson V H *et al.* A cluster of mutations within a short triplet repeat in the C1 inhibitor gene. *Proc Natl Acad Sci USA* 1994; **91**: 9622-5.
16. Cicardi M, Igarashi T, Kim M S, Frangi D, Agostoni A, Davis III A E. Restriction fragment length polymorphism of the C1 inhibitor gene in hereditary angioneurotic edema. *J Clin Invest* 1987; **80**: 1640-3.
17. Siddique Z, McPhaden A R, Whaley K. Characterisation of nucleotide sequence variants and disease-specific mutations involving the 3' end ofthe C1-inhititor gene in hereditary angio-oedema. *Hum Hered* 1995; **45**: 98-102.
18. Siddique Z, McPhaden A R, Fothergill J E, Whaley K. A point mutation in the C1-inhibitor gene causes type I hereditary angioedema. *Hum Hered* 1993; **43**: 155-8.
19. Donaldson V H, Bissler J J. C1-inhibitors and their genes: an update. *J Lab Clin Med* 1992; **119**: 330-3.
20. Donaldson V H. C1-inhibitor and its genetic alterations in hereditary angioneurotic edema. *Int Rev Immunol* 1993; **10**: 1-16.
21. Donaldson V H, Rosen F S. Hereditary angioneurotic edema: a clinical survey. *Pediatrics* 1966; **37**: 1017-27.
22. Cicardi M, Bergamaschini L, Marasini B, Boccassini G, Tucci A, Agostoni A. Hereditary angioedema: an appraisal of 104 cases. *Am J Med Sci* 1982; **284**: 2-9.

23. Stiller R J, Kaplan B M, Andreoli J W. Hereditary angioedema and pregnancy. *Obstet Gynaecol* 1984; **64**: 133-5.

24. Chhibber G, Cohen A, Lane S, Farber A, Meloni F J, Schmaier A H. Immunoblotting of plasma in a pregnant patient with hereditary angioedema. *J Lab Clin Med* 1990; **115**: 112-21.

25. Chappatte O, De Swiet M. Hereditary angioneurotic oedema and pregnancy. Case reports and review of the literature. *Br J Obstet Gynaecol* 1988; **95**: 938-42.

26. Cunningham D S, Jensen J T. Hereditary angioneurotic edema in the puerperium. *J Reprod Med* 1991; **36**: 312-3.

27. Postnikoff I M, Pritzker K P. Hereditary angioneurotic edema: an unusual cause of maternal mortality. *J Forensic Sci* 1979; **24**: 473-8.

28. Cohen A J, Laskin C, Tarlo S. C1 esterase inhibitor in pregnancy. *J Allergy Clin Immunol* 1992; **90**: 412-3.

29. Gordon E M, Ratnoff O D, Saito H, Donaldson V H, Pensky J, Jones P K. Rapid fibrinolysis, augmented Hageman factor (factor XII) titers and decreased C1 esterase inhibitor titers in women taking oral contraceptives. *J Lab Clin Med* 1980; **96**: 762-9.

30. Warin R P, Cunliffe W J, Greaves M W, Wallington T B. Recurrent angioedema: familial and oestrogen-induced. *Br J Dermatol* 1986; **115**: 731-4.

31. Pickering R J, Kelly J R, Good R A, Gewurtz H. Replacement therapy in hereditary angioedema. Successful treatment of two patients with fresh frozen plasma. *Lancet* 1969; **1**: 326-30.

32. Sim T C, Grant J A. Hereditary angioedema: its diagnosic and management perspectives. *Am J Med* 1990; **88**: 656-64.

33. Gadek J E, Hosea S W, Gelfand J A et al. Replacement therapy of hereditary angioedema. Successful treatment of acute episodes of angioedema with partly purified C1-inhibitor. *New Engl J Med* 1980; **302**: 542-6.

34. Frank M M. Effect of sex hormones on the complement-related clinical disorder of hereditary angioedema. *Arthritis Rheum* 1979; **22**: 1295-9.

35. Gelfand J A, Sherins R J, Alling D W, Frank M M. Treatment of hereditary angioedema with danazol. reversal of clinical and biochemical abnormalities. *New Engl J Med* 1976; **95**: 1444-8.

36. Pitts J S, Donaldson V H, Forristal J, Wyatt R J. Remissions induced in hereditary angioneurotic edema with an attenuated androgen (danazol): correlation between concentrations of Cl-inhibitor and the fourth and second components of complement. *J Lab Clin Med* 1978; **92**: 501-7.

37. Cicardi M, Bergamaschini L, Cugno M, Hack E, Agostoni G, Agostoni A. Long-term treatment of hereditary angioedema with attenuated androgens: a survey of a 13-year experience. *J Allergy Clin Immunol* 1991; **87**: 768-73.

38. Hosea S W, Santaella M L, Brown E J, Berger M, Katusha K, Frank M M. Long-term therapy of hereditary angioedema with danazol. *Ann Intern Med* 1980; **93**: 809-12.

39. Donaldson V H. Danazol. *Am J Med* 1989; **87**: (3-49N-55N).

40. Sheffer A L, Fearon D T, Austen K F. Clinical and biochemical effects of stanazol therapy for hereditary angioedema. *J Alllergy Clin Immunol* 1981; **68**: 181-7.

41. Blomé G. Treatment of hereditary angioneurotic oedema with tranexamic acid. a random double-blind cross-over study. *Acta Med Scand* 1972; **192**: 293-8.

42. Frank M M, Sergent J S, Kane M A, Alling D W. Epsilon aminocaproic acid therapy of hereditary angioneurotic edema: a double-blind study. *New Engl J Med* 1972; **286**: 808-812.

43. Galan H L, Reedy M B, Starr J, Knight A B. Fresh frozen plasma prophylaxis for hereditary angioedema during pregnancy. A case report. *J Reprod Med* 1996; **41**: 541-4.

44. Boulos A N, Brown R, Hukin A, Williams R M. Danazol prophylaxis for delivery in hereditary angioneurotic oedema. *Br J Obstet Gynaecol* 1994; **101**: 1094-5.

45. Raychaudhuri K, Buck P, Pumphrey R S H. Termination of pregnancy in a patient with hereditary angioedema. *Br J Hosp Med* 1997; **58**: 287-8.

46. Jaffe C J, Atkinson J P, Gelfand J A *et al.* Hereditary angioedema: the use of fresh frozen plasma for prophylaxis in patients undergoing oral surgery. *J Allergy Clin Immunol* 1975; **55**: 385-93.

47. Cox M, Holdcroft A. Hereditary angioneurotic oedema: current management in pregnancy. *Anaesthesia* 1995; **50**: 547-9.

The Ulster Medical Journal, Volume 69, No. 1, pp. 58-60, May 2000.

Case Report

Primary squamous carcinoma of the Thyroid

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Accepted 14 January 2000

Primary squamous carcinoma of the thyroid gland is a rare condition accounting for less than 1% of all thyroid malignancies.[1,2] Although most frequently seen in the fifth and sixth decades, the tumour may arise in patients across a wide age distribution.[3] Squamous carcinoma of thyroid is associated with a poor prognosis, most patients dying within one year of diagnosis.[1,3] Overall, metastatic squamous carcinoma involving the thyroid is more common than the development of a primary tumour. It is therefore mandatory, when squamous carcinoma is identified within the thyroid, to exclude the possibility of a primary tumour elsewhere before concluding that the neoplasm is arising *de novo* within the gland.

CASE REPORT A 48-year-old male presented to an ENT Clinic because of pain in the left ear, a sore throat, a lump on the left side of his neck and hoarseness. On examination he had a "breathy" voice and was unable to produce a normal explosive cough. Palpation of the neck revealed a hard lymph node in the left upper cervical chain and a left sided goitre.

Indirect laryngoscopy confirmed a paralysed left vocal cord and computed tomography demonstrated a mass in the left lobe of thyroid, with displacement of the trachea and oesophagus to the right. In addition, multiple enlarged lymph nodes in the region of the left carotid sheath were identified. Isotope scintigraphy of the thyroid showed a non-functioning nodule almost completely replacing the left lobe of the gland. Fine needle aspiration for cytology revealed poorly differentiated carcinoma.

The patient was admitted for surgical exploration of the neck. At operation the right thyroid lobe was grossly normal. Multiple enlarged lymph nodes were easily palpable on the left side of the neck and the left thyroid lobe was replaced by a hard tumour mass. Wedge biopsy was performed and frozen section examination was reported as showing "carcinoma, probably anaplastic". Total thyroidectomy was carried out, although it was recognised that there was residual tumour present along the left lateral border of both the trachea and oesophagus. The left lateral neck was now opened and a formal modified radical neck dissection carried out with removal of all tissue from a level above the clavicle up to the angle and lower border of the mandible. Multiple metastatic nodes were removed. The lymph nodes in the midneck were densely adherent to the internal jugular vein and the vein was therefore transfixed and resected in continuity. Following the procedure, all gross tumour in the left lateral neck had been removed. Post-operatively the patient progressed satisfactorily and without major complication.

Fig a. Photomicrograph showing normal thyroid tissue (arrow) and invading poorly differebtiated squamous carcinoma.

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Definitive histopathology revealed poorly differentiated tumour, composed of collections of large pleomorphic cells (Figure). There was evidence of both lymphovascular invasion and perineural spread. The tumour cells were largely negative on immunostaining for thyroglobulin and the neuroendocrine markers calcitonin and chromogranin A. Foci of keratinisation were identified and the overall features suggested a diagnosis of primary squamous cell carcinoma of thyroid with nodal metastases.

Barium meal and CT scanning of the chest revealed no evidence of a primary tumour within the oesophagus or lung fields, and comprehensive ENT assessment was negative. The patient was commenced on thyroxine 100 ug daily, and following consultation with the oncologists, commenced a course of radical radiotherapy to the left side of his neck.

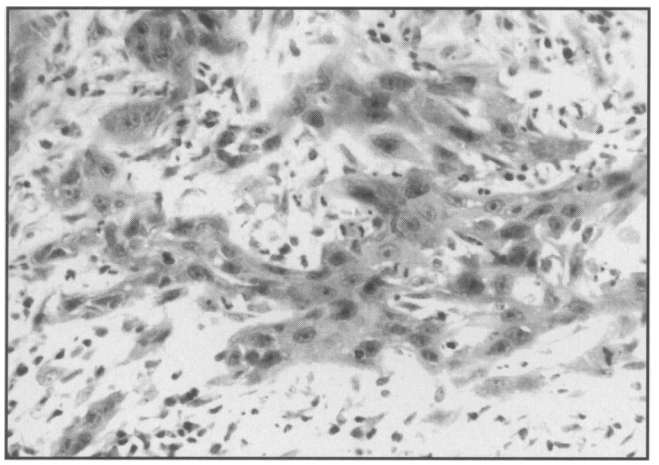

Fig b. High power view of poorly differentiated squamous carcinoma.

At three month review a hard mobile mass was detected in the patient's left axilla and he was therefore readmitted and axillary clearance carried out. The histology report revealed poorly differentiated carcinoma within multiple lymph nodes. Repeat CT scan of the chest and upper abdomen now demonstrated wide-spread metastatic deposits throughout both lung fields and a solitary liver metastasis. In light of these findings a course of cisplatin was advised and administered.

Unfortunately, the patient developed dysphagia, and a stricture at the level of the previous thyroid surgery was confirmed radiologically. His general condition and his swallowing deteriorated further and palliative gastrostomy was carried out. The patient died eight months after his initial operation.

DISCUSSION

Primary squamous cell carcinoma of the thyroid is a rare but aggressive tumour which must be distinguished from papillary and follicular carcinoma, each of which is associated with good prognosis. Squamous metaplasia may occasionally be seen within papillary cancers.[4] Histologically, squamous carcinoma of thyroid may be 'pure' or demonstrate both squamous and glandular elements.[2,4] When squamous carcinoma is diagnosed, the possibility of the tumour arising from an adjacent structure such as the oesophagus, or representing a metastasis from a primary growth elsewhere, must be considered.

Speculation regarding the origin of squamous carcinoma of the thyroid includes the suggestions that the neoplasm arises from thyroglossal duct remnants, develops following squamous metaplastic change within thyroiditis or occurs as a consequence of transitional changes in differentiated or anaplastic thyroid cancer.[2,4,5] In our patient, histological examination of the specimen revealed a poorly differentiated tumour with collections of large pleomorphic cells and foci of keratinisation – features of squamous cell carcinoma (Figure). These findings were present in both the left lobe of thyroid and the resected lymph nodes.

Frequently, patients with squamous cell carcinoma present with advanced local disease, which may include invasion of muscle, trachea, great vessels and other organs thus rendering excision difficult or impossible. Distant metastases, especially to the lungs, are often present at diagnosis or appear shortly thereafter. Patients with well differentiated tumours fare no better than those with poorly differentiated lesions and few individuals survive one year.[3] Shimaoka and Tsukada reported a better prognosis for patients with adenosquamous cancers when compared to patients with 'pure' squamous cell tumours, particularly if the squamous component was only a minor part of a predominantly papillary or follicular adenocarcinoma.[4]

The few patients with long term survival reported in the literature have undergone radical surgery alone or in combination with radiotherapy.[3] To date chemotherapy has not been shown to be of benefit in this condition. Simpson & Caruthers

noted no benefit in two patients treated with adriamycin nor in another treated with 5-fluorouracil and mitomycin,[3] while Shimaoka & Tsukada failed to achieve a response in three patients treated with nitrogen mustard, vincristine and AB-132, respectively.[4]

Cisplatin has been shown to have benefited patients suffering from other squamous cell cancers of the head and neck [6] but, to date, no information is available on its use in squamous carcinoma of thyroid. On the basis of current knowledge and the limited reported experience in dealing with this unusual tumour, we advise a radical surgical approach for the patient in whom primary squamous carcinoma of thyroid is diagnosed. Total thyroidectomy and resection of all gross tumour should be attempted and if advanced local disease is present, then maximum possible debulking should be performed. Metastatic lymph nodes in the lateral neck should be dealt with by formal neck dissection, sparing the internal jugular vein and sternomastoid muscle if possible. In the absence of systemic metastases, conventional wisdom would suggest that adjunctive external irradiation to the neck and superior mediastinum is appropriate but the usefulness of supplementary chemotherapy in these unfortunate patients is, to date, unsubstantiated.

REFERENCES

1. Korovin G, Kuriloff D, Cho H, Sobol S. Squamous cell carcinoma of the thyroid – a diagnostic dilemma. *Ann Otol Rhinol Laryngol* 1989; **98**: 59-65.
2. Harada T, Shimaoka K, Katagiri M, Shimizu M, Hosoda Y, Ito K Rarity of squamous cell carcinoma of the thyroid: autopsy review. *World J Surg* 1994; **18**: 542-6.
3. Simpson J, Carruthers J. Squamous cell carcinoma of the thyroid gland. *Am J Surg* 1998; **156**: 44-6.
4. Shimoaka K, Tsukada Y. Squamous cell carcinomas and adenosquamous carcinomas originating from the thyroid gland. *Cancer* 1980; **46**: 1833-42.
5. Harcourt-Webster J. Squamous epithelium in the human thyroid gland. *J Clin Pathol* 1996; **19**: 384-8.
6. Planting A S, de Mulder P H, de Graeff A, Verweij J. Phase II study of weekly high-dose cisplatin for six cycles in patients with locally advanced squamous cell carcinoma of the head and neck. *Eur J Cancer* 1997; **33**: 61-5.

The Ulster Medical Journal, Volume 69, No. 1, pp. 61-62, May 2000.

Case Report

An unusual case of late graft infection

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Accepted 20 January 2000

The incidence of vascular prosthetic graft infection is relatively uncommon (ranging from 2-5%),[1] but the management of this condition still poses a major challenge to vascular surgeons. The majority of graft infections are felt to be related to bacterial implantation at the time of original surgery. We report on a case of late graft infection with an unusual cause.

CASE REPORT A sixty-two-year old lady presented with a four month history of gradual onset of left iliac fossa (LIF) and groin pain associated with tiredness, poor appetite and weight loss. She had a history of aorto-bifemoral bypass grafting eight years previously for occlusive aortic disease. The patient was apyrexic but tender in the LIF with a fullness in the left groin. All peripheral pulses were present. Initial blood investigations revealed a normal white cell count with an ESR of 97 mm/hr. The right kidney was found to be hydronephrotic on ultrasound. CT scan demonstrated abnormal tissue and gas around the graft confirming infection. Arteriography confirmed graft patency.

At surgery, bilateral axillo-femoral bypass grafts were initially constructed. Laparotomy was then carried out. The appendix was found to be necrotic and adherent to the right pelvic wall. The peritoneum covering the graft on the lateral pelvic wall appeared intact, but further dissection revealed that the appendix was acutely inflamed and directly adherent to the right limb of the infected graft. Pus from the para-aortic area did not yield bacterial growth. The pathologist reported acute transmural inflammation of the appendix. The patient had an uneventful recovery after primary graft excision; she remains well two years later.

DISCUSSION

Graft infection may present early (within thirty days of surgery) or up to several years after implantation.[1] Transient bacteraemia may lead to graft infection, but occult seeding at the time of surgery is felt to be the more common mechanism. Factors associated with higher risk of infection include emergency surgery, re-operation, haematoma formation and the presence of distant infection. Coagulase negative staphylococcus aureus has emerged as the most commonly identified pathogen, but often no bacterial growth is identified,[2] even in the presence of overt pus. For aortic graft infection the associated mortality rate has been reported as high as 70% with an amputation rate of 11 to 57%.[3-5] Aggressive treatment is thus justified.

Graft infection in this particular case seems to have been caused by acute appendicitis. There have been no previous reports of such an event in the literature. The case is also unusual because of the prolonged time interval (eight years) between graft implantation and the development of infection.

REFERENCES

1. Bandyk D F, Esses G E. Prosthetic graft infection. *Surg Clin N Am* 1994; **74**: 571 -89.
2. Sharp W J, Hoballah J J, Mohan C R, Kresowik T F, Martinasevic M, Chalners R T A, Carson, J D. The management ofthe infected aortic prosthesis: a current decade of experience. *J Vasc Surg* 1994; **19**: 884-50.

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3. Calligaro K, DeLaurentis D, Veith F. An overview of the treatment of infected prosthetic vascular grafts. *Adv Surg* 1996; **29**: 3-16.

4. Hannon R J, Wolfe J H N, Mansfield A O. Aortic prosthetic infection: 50 patients treated by radical or local surgery. *Br J Surg* 1996; **83**: 654-8.

5. Naylor A R, Clark S, London N J M, Sayers R D, Macpherson D S, Barrie W W, Bell P R F. Treatment of major aortic graft infection: preliminary experience with total graft excision and in situ replacement with rifampicin bonded prosthesis. *Eur J Vasc Endovasc Surg* 1995; **9**: 252-6.

The Ulster Medical Journal, Volume 69, No. 1, pp. 63-64, May 2000.

Case Report

Diagnostic dilemma of hyperamylasaemia in acute abdominal emergencies

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Accepted 28 February 2000

Measurement of serum amylase is commonly used to diagnose acute pancreatitis. Moderate hyperamylasaemia is frequently seen both in acute pancreatitis and other conditions causing acute abdominal pain such as mesenteric infarction.[1,2] However, grossly elevated serum amylase levels (>five times normal) are rare in non-pancreatic causes of abdominal pain.[3] We report two cases of mesenteric infarction with serum amylase levels greater than ten times normal.

CASE REPORTS

Case 1 An 85 year old lady presented with a short history of severe generalised abdominal pain. She had a tachycardia of 125/min and was hypotensive (BP 59/38mmHg) with right iliac fossa and epigastric tenderness and normal bowel sounds.

Serum amylase was 2876 IU/L (range 0-220). White cell count was 14 x 10^9/L and she was acidotic with a pH of 7.16 (pC02 6.9Kpa, pO2 6.9Kpa and HCO3 18.7mmol/L). Other blood parameters were normal. Erect chest and abdominal radiographs revealed no abnormality. A diagnosis of acute pancreatitis was made.

Despite resuscitation efforts she died six hours following admission. Autopsy confirmed ischaemic gangrene of the terminal ileum, caecum, ascending and proximal transverse colon. The pancreas was normal.

Case 2 A 75 year old man was admitted six weeks following a laparoscopic cholecystectomy with severe upper abdominal pain. He was haemodynamically stable and had epigastric tenderness with reduced bowel sounds.

White cell count was 21 x 10^9/L, glucose 11.8 mmol/L). Serum amylase was 4861 IU/L (range 0-220). Other blood parameters were normal. An erect chest and abdominal radiographs were unremarkable. A diagnosis of acute pancreatitis was made.

He was treated conservatively but over the next 48 hours he deteriorated and was transferred to the intensive care unit. But he died before a contrast enhanced CT scan could be performed. Autopsy revealed 135 cm of infarcted ileum, secondary to a band adhesion causing strangulation. The pancreas was normal.

DISCUSSION

Elman *et al* in 1929 demonstrated that a raised serum amylase has a diagnostic value in acute pancreatitis, and it remains the most widely used diagnostic test of acute pancreatitis.[4] Moderate hyperamylasaemia has been reported in numerous extrapancreatic causes of acute abdominal pain such as acute cholecystitis, ischaemic bowel, perforated viscus, ruptured ectopic pregnancy and ruptured abdominal aortic aneurysms.[1,2] Chase *et al* reported that 13% of patients presenting with acute abdominal pain of non pancreatic origin had a moderately elevated serum amylase.[2] Hyperamylasaemia of greater than five

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times the upper limit of normal is highly specific for pancreatitis and often considered diagnostic and is rarely seen in extrapancreatic causes of acute abdominal pain.[3]

Since markedly elevated serum amylase levels (>5 times normal) are not always associated with acute pancreatitis, new biochemical tests and radiological imaging modalities such as ultrasound, CT and MRI maybe helpful diagnostic aids. Previous investigators have concluded that using a combination of biochemical assays, such as amylase, lipase and trypsin, does not clearly improve the diagnostic accuracy.[5] Ultrasonography adequately visualises the pancreas in only 60 to 70% of patients with acute pancreatitis.[6] The diagnostic accuracy of computed tomography (CT) is much better. Ninety percent of contrast enhanced CT scans performed within 72 hours of admission tend to be abnormal in patients with acute pancreatitis.[7]

Recent guidelines from the British Society of Gastroenterology suggest CT scanning in acute pancreatitis should be performed when the diagnosis is uncertain, for assessment of severe cases (within 3-10 days) and when clinical deterioration occurs.[4] Our experience suggests that mesenteric infarction can produce markedly raised serum amylase levels, and early contrast enhanced CT scanning should be considered more readily in order to help confirm the diagnosis and prevent inappropriate non-operative treatment of mesenteric infarction.

REFERENCES

1. Lang E, Afilialo M, Dankoff J, Colacone A, Tselios C, Guttmann A. The prognostic significance of moderate hyperamylasemia in the evaluation of the emergency department patient. *J Emerg Med* 1995; **13**: 107-12.
2. Chase C W, Barker D E, Russel W L, Burns R P. Serum amylase and lipase in evaluation of acute abdominal pain. *Am Surg* 1996; **62**: 1028-33.
3. Hendry W S, Thomson S R, Scott S T, Davidson A I. Significant hyperamylasaemia in conditions other than acute pancreatits. J *R Coll Surg Edinb* 1987; **32**: 213-15.
4. Elman R, Arneson N, Graham E A. Value of blood amylase estimation in diagnosis of pancreatic disease a clinical study. *Arch Surg* 1929; **19**: 943-67.
5. Werner M, Steinberg W M, Pauley C. Strategic use of individual and combined engyme indicators for acute pancreatitis analysed by receiver-operator characteristics. *Clin Chem* 1989; **35**: 967-71.
6. McKay A J, Imrie C W, O'Neill J, Duncan J G. Is an early ultrasound scan of value in acute pancreatitis? *Br J Surg* 1982; **69**: 369-72.
7. London N J M, Neoptolemos J P, Lavelle J *et al.* Serial computed tomography scanning in acute pancreatitis: a prospective study. *Gut* 1989; **30**: 397-403.
8. Glazer G, Imrie C W, Mann D V. United Kingdom guidelines for the management of acute pancreatitis. *Gut* 1998; **42** (suppl 2): S1-S13.

The Ulster Medical Journal, Volume 69, No. 1, pp. 65-68, May 2000.

Case Report

Benign liver lesions in female patients

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Accepted 20 December 1999

Liver cell adenoma and focal nodular hyperplasia are benign conditions, often encountered in young and middle aged female patients. They can present acutely, but more often are diagnosed incidentally during investigation of abnormal liver function tests or vague abdominal pain. We present four cases, which contrast the diagnosis and management of focal nodular hyperplasia (FNH) and liver cell adenoma (LCA).

CASE 1

A 33-year-old previously healthy woman was admitted with sudden onset of epigastric and left upper abdominal pain. Her only regular medication was the oral contraceptive pill, used almost continuously for the previous sixteen years. Ultrasound and CT scans were performed. These revealed a large mass in the left lobe of the liver into which bleeding had occurred (Fig. 1). In addition there was a large lesion in the posterior aspect of the right lobe. Appearance on CT scan was in keeping with a ruptured lesion in the left lobe and focal nodular hyperplasia in the right lobe. Laparotomy revealed a large tumour in segments II and III with some surrounding satellite nodules. There was evidence of haemorrhage into the tumour and a haematoma, was present in the left upper quadrant. Left hepatic lobectomy was performed. Histopathology confirmed the left lobe lesion to be a liver adenoma; biopsy of the right lobe lesion revealed focal nodular hyperplasia. She remains well three years following surgery. Repeat CT scan at two years has demonstrated no change in size of the right lobe lesion.

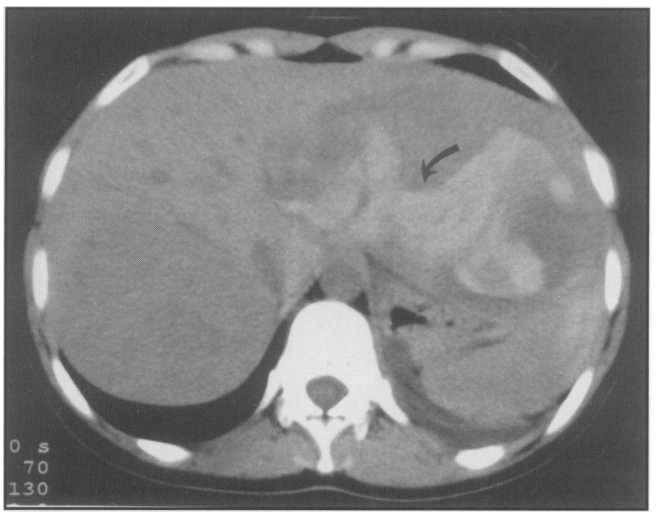

Fig 1. CT scan, from patient 1, demonstrating a large heterogeneous lesion in the left lobe, into which bleeding has occurred (curved arrow).

CASE 2

A 26-year-old woman with a three year history of oral contraceptive use presented with a three-month history of right-sided abdominal pain. Clinical examination was unremarkable but USS of the abdomen showed a 5 x 7 x 8 cm hyperechoic mass in the right lobe of the liver. Contrast enhanced CT scan demonstrated the same lesion and the presence of a central scar. On repeat CT imaging six months later no significant change was seen. This is consistent with a diagnosis of focal nodular hyperplasia. Eighteen months after initial presentation she remains well.

CASE 3

A 29-year-old woman was admitted electively for laparoscopic cholecystectomy. During initial laparoscopy a tumour arising from the left lobe of the liver was noted. Conversion to open cholecystectomy allowed routine cholecystectomy and biopsy of the liver lesion to be performed. Histopathology was consistent with focal nodular hyperplasia. An enhanced CT scan,

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one month after surgery, revealed no focal hepatic abnormality. In the succeeding months, the patient experienced episodes of epigastric pain. A further CT scan six months after surgery identified a 3.8 cm diameter lesion in the left lobe with no central scar or internal haemorrhage. A third CT scan eighteen months after her initial surgery showed no change. However the patient was experiencing intermittent episodes of abdominal pain. This fact, combined with her desire to have a further child in the future, resulted in elective surgery to enucleate the FNH lesion from segment IV of the liver.

CASE 4

A 54-year-old woman was noted to have abnormal liver function tests on routine investigation of abdominal pain. Her only past medical history was essential hypertension, treated with thiazide diuretics. She had lived in Australia and had travelled to the Far East, but had no known history of hepatitis. Ultrasound revealed a 6 x 4 cm mass in the posterior aspect of the right lobe of the liver. This was irregular in outline, and mainly echogenic but with an echo-poor centre. CT scan showed a well-defined mass measuring 5 x 6 x 5 cm, which was hypodense with a central stellate scar (Fig.2). The appearances were consistent with FNH. CT guided biopsy was performed. The histology revealed unremarkable hepatic architecture, and the biopsy was not diagnostic of FNH from the material submitted. Repeat CT scan 8 months after the initial investigations showed no significant change. The patient has remained well two years later.

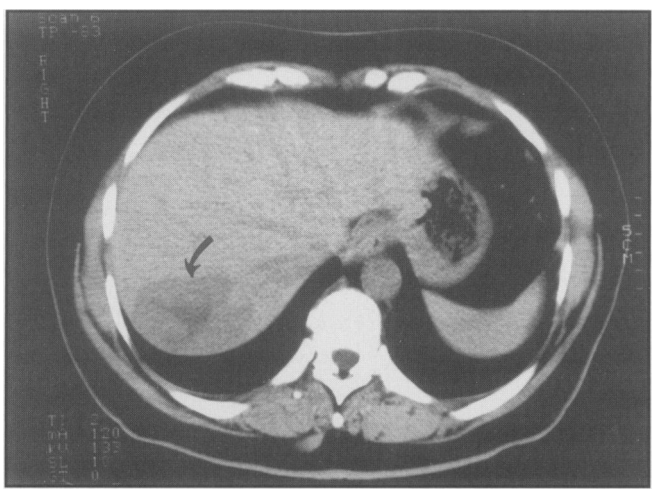

Fig 2. CT scan, from patient 4, demonstrating a hypodense mass in the right lobe, with a central stellate scar (curved arrow).

DISCUSSION

The association between the development of liver cell adenoma (LCA) and the use of oral contraceptives was first reported in 1973.[1] Early reports estimated that the risk of developing LCA increases thirty four fold in women using high oestrogen oral contraceptives.[2] Recent studies for low dose oestrogen contraceptives showed the risk to be increased only by a factor of three.[3] Prolonged duration of oral contraceptive use increases the risk of liver cell adenoma. One study demonstrated that use of oral contraceptives for five, nine or greater than nine years increases the risk by 2, 5, 7.5 and 25 respectively.[4] In contrast, focal nodular hyperplasia (FNH), although more common than LCA, is not associated with the use of oral contraceptives and the increased incidence in the past twenty five years is likely to be due to increased awareness and the more widespread use of ultrasound.[5]

The natural history of these conditions varies. LCA carries a significant risk of complications such as rupture, haemoperitoneum, shock, death and, rarely, malignant transformation.[6] FNH however is essentially benign. It is not premalignant and complications such as massive growth, rupture or haemorrhage are rare.[5] In the few reported cases with haemorrhage the histological diagnosis of FNH has been questioned.[6] This fundamental difference in long term behaviour influences the presentation and management of the two conditions.

Case 1 is typical of LCA. Eighty percent of patients with hepatic adenoma are symptomatic – half of these have signs related to a mass, such as pain, whilst the other half are symptomatic because of haemorrhage. This may be intratumoural, subcapsular or intraperitoneal. Essentially the reverse is true in FNH. Typically, only 10% of this group have symptoms, the lesion being found incidentally in the remaining 90%, as in cases 3 and 4.[7] In one case series, no patient with FNH had presented with rupture or bleeding.[8]

Radiological imaging alone is not always diagnostic, but nonetheless can help in differentiating FNH from LCA. The presence of an avascular central stellate scar, although not always found, is pathognomonic for FNH when it occurs, since it never arises in liver cell adenoma.[7] Similarly, precontrast hyperdense areas (haemorrhage) is supportive of the diagnosis of LCA. Differentiation can also be made with less

widely available imaging techniques. These include MRI with or without gadolinium enhancement, colour doppler ultrasound and radionuclide scintigraphy, with Technetium (Tc 99) sulphur colloid.

With MRI the central stellate area of FNH is hyperintense on T2 and hypointense on T1 images. Enhancement with gadolinium shows accumulation of contrast agent within the central area on delayed T1 images. For LCA, haemorrhage is hyperintense on T1 and T2 images, while necrosis is hyperintense on T2 and hypointense on T1 images. Characteristically LCA shows no accumulation of gadolinium contrast agent within the tumour.[9]

With colour doppler FNH shows arterial signals within the tumour, while LCA demonstrates venous signals. Using radio labelled colloid a focal defect is seen in LCA, compared to increased or normal uptake in FNH.[9] This stems from the histolgical difference of these lesions. LCA lacks Kupffer cells, and does not take up radioisotope. In FNH Kupffer cells are present and metabolically active resulting in increased uptake.[7]

Histologically these lesions differ.[10] Macroscopically, LCA is yellowish tan in colour with a homogeneous appearance. There is no true capsule but a pseudocapsule may be created by the compression of normal liver parenchyma. Haemorrhage, both macroscopic and microscopic, is common. Macroscopically, lobulation and a central scar are characteristic of FNH. Microscopically Kupffer cells and bile ducts are found in FNH, but are absent in LCA, which is distinguished by the presence of glycogen rich vacuoles. However, differentiation and definite diagnosis on percutaneous biopsy is often difficult as the tumour, particularly FNH, can so closely resemble normal liver parenchyma. Case 4 illustrates this point well, as the radiological diagnosis of FNH was not conclusively supported by percutaneous biopsy. Percutaneous biopsy is considered safe, but complications including haemorrhage and death do occur. However mortality rates following the procedure are extremely low (0.03-0.006%).[11] Imaging and histology, along with the clinical history may all be used to make the diagnosis of LCA or FNH. This is important because, the natural history of the two conditions differs markedly and so, therefore, does their management.

Discontinuation of oral contraceptives is obligatory in patients with LCA. Although occasionally regression has been observed after discontinuation this is not invariable, and growth, rupture and malignant transformation have been reported, despite cessation of contraceptive use.[7, 12] Most authors agree that oral contraceptives are not the causal agent of FNH. However, it has been postulated that they might have a trophic effect increasing the size and vascularity. Therefore, discontinuation of oral contraceptives is also advised in this condition.

The management of FNH requires a flexible approach. Asymptomatic lesions are best managed expectantly and can be safely observed with regular ultrasound. The only clear indications for surgery are the presence of symptoms or uncertainty about the diagnosis. In the latter case, if resection is a major hazard biopsy alone is recommended since the prognosis of FNH left undisturbed is excellent. For symptomatic FNH, resection has been demonstrated to be safe with no operative mortality and less than 1% morbidity. Relief of symptoms is also generally achieved.[13] A further indication for resection of FNH is planned pregnancy, if the tumour is easily accessible. This is because it has been well documented that these lesions may increase in size during pregnancy.[14] It is for these reasons that patient 3 underwent elective surgery. The diagnosis of LCA strongly supports surgical intervention, due to long term risks of conservative management. Elective resection of LCA is almost as safe as FNH, morbidity and mortality for this being 7% and less than 1% respectively. This increases to 5-8% for emergency resection.[5]

In summary, FNH and LCA are liver masses identified in women and the latter is clearly increased by use of oral contraceptive steroids. They differ in histological and radiological characteristics and these are often of use in making a diagnosis. While FNH is often asymptomatic and benign, LCA is, by contrast, often symptomatic with a potential for significant complications. These risks inherent in LCA make surgical intervention in this condition the treatment of choice.

REFERENCES

1. Baum J K, Bookstein J J, Holz F, and Klein E W. Possible association between benign hepatomas and oral contraceptives. *Lancet* 1973; **2**: 926-9.

2. Rooks J B, Ory H W, Ishak G, Strauss L T, Greenspan J R, Paganini A H, Twyler C W: Epidemiology of hepatoeellular adenoma, the role of oral contraceptive use. *JAMA* 1979; **242**: 644-8.

3. Flejou J F, Pignon J P, LE M G, Belghiti J, Barge J, Bismuth H, Benhamou J P. Liver cell adenoma, focal nodular hyperplasia and oral contraceptive use: a French case-control study in young women. (Abstract) *Hepatology* 1994; **20**: [Prog. Issue] 280A. No. 736.

4. Edmondson H A, Henderson B, and Benton B. Liver-cell adenomas associated with use of oral contraceptives. *N Engl J Med* 1976; **294**: 470-2.

5. Nagoney D M. Benign hepatic tumours: focal nodular hyperplasia or hepatocellular adenoma. *World J Surg* 1995; **19**: 13-8.

6. Mays E T, Christorpherson W M, Mahr M M, Williams H C. Hepatic changes in young women ingesting contraceptive steroids: hepatic haemorrhage and primary hepatic tumors. *JAMA* 1976; **235**: 730-2.

7. Shortell C K, Schwartz S I. Hepatic adenoma and focal nodular hyperplasia. *Surg Gynecol Obstet* 1991; **173**: 466-31.

8. Foster J H, Beman M. Solid liver tumours. 1977; W B Saunders. Philadelphia.

9. Cherqui D, Rahmouni A et al. Management of focal nodular hyperplasia and hepatocellular adenoma in young women: a series of 41 patients with clinical, radiological and pathological correlations. *Hepatology* 1995; **22**: 1674-81.

10. Knowles D M. Casarella W J, Johnson P M, Wolff M. The clinical, radiologic and pathologic characterization of benign hepatic neoplasms. *Medicine* 1978; **57**: 223-37.

11. Complications in Diagnostic Imaging and Interventional Radiology (3rd Edit) 1996, Blackwell Science. George Ansell, Michael Betterman p503-07.

12. Gyorffy E, Bredfeldt J E, Black W C. Transformation of hepatic cell adenoma to hepatocellular carcinoma due to oral contraceptive user. *Ann Intern Med* 1989, **110**: 489-90.

13. Iwatsuki S, Todo S, Starzl T E. Excisional therapy for benign hepatic lesions. *Surg Gynecol Obstet* 1990; **171**: 240-6.

14. Scott L D, Katz A R, Duke J H, Cowan D F, Maklad N F. Oral contraceptives, pregnancy and focal nodular hyperplasia of the liver. *JAMA* 1984; **251**: 1461-3.

The Ulster Medical Journal, Volume 69, No. 1, pp. 69-70, May 2000.

Case Report

Bouveret's syndrome: gallstone ileus causing gastric outlet obstruction

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Accepted 8 December 1999

CASE REPORT A 71-year-old lady presented with acute cholecystitis which settled with conservative treatment. She was readmitted four months later with another attack of acute cholecystitis. Three days after admission she began to vomit repeatedly. She had a positive succussion splash consistent with a diagnosis of gastric outlet obstruction. She was treated initially with nasogastric aspiration and intravenous fluids. A plain abdominal X-ray showed a large opacity in the upper abdomen to the right of the midline (Fig). A barium meal revealed a cholecystoduodenal fistula containing a large calculus which was causing partial gastric outlet obstruction. The radiological features were confirmed at laparotomy. A 6 cm gallstone was retrieved.

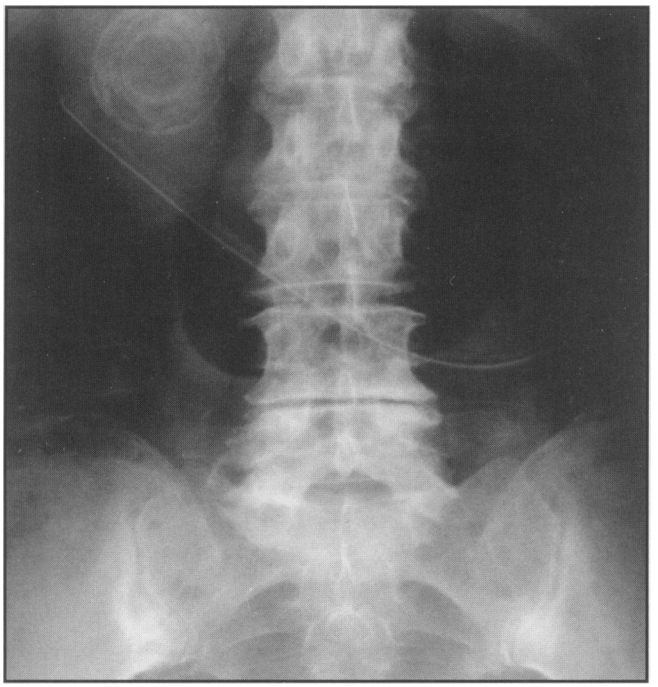

Fig. Plain abdominal X-ray demonstrating nasogastric tube and a large "doughnut" shaped calcified opacity on the right side of the first lumbar vertebra.

Following dissection of the fistula the duodenal defect was too large to allow primary closure and therefore a distal gastrectomy (Polya) was performed and the duodenal stump closed. A cholecystectomy was also performed. The patient made a slow recovery, due to delayed gastric emptying, but was discharged 26 days post-operatively.

DISCUSSION

Gastric outlet obstruction due to the passage of a gallstone from the gallbladder to the duodenum through a cholecystoduodenal fistula is a rare condition. Though described in two patients at autopsy by Bonnet in 1841, Bouveret made the first pre-operative diagnosis in 1896 and defined the syndrome. Since Bouveret's description only approximately 240 cases have been reported in the literature worldwide.[1]

After passing through the fistula, gallstones less than 2.5 cm in diameter migrate through the bowel and may impact in the terminal ileum producing the classical gallstone ileus. Stones larger than this are more likely to impact in the duodenum.

The majority of patients with this condition are elderly females with a history of biliary disease who present with abdominal pain and non-bilious vomiting.

Plain abdominal X-ray is diagnostic in 23% of cases when pneumobilia and a calculus on the

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right side of T12/L1 vertebrae are present. Oral contrast studies reveal the diagnosis in 45% of cases, but upper gastrointestinal endoscopy is 60% sensitive and can be therapeutic in 7% of patients. For high risk elderly patients Holl has advocated extracorporeal shock-wave lithotripsy with endoscopic extraction of the fragments.[2]

Surgery is indicated in 93% of patients. The preferred operation is a one-stage procedure with removal of the ectopic stone, closure of the fistula and cholecystectomy. At the time of surgery the rest of the bowel should be examined to exclude other stones. Alternatively a two-stage procedure can be performed with stone extraction initially, and closure of the fistula at a later date if symptoms occur. If the fistula is not closed there is a risk of cholangitis, carcinoma of the gallbladder and recurrent ileus.[3] The mortality from this condition is 12%.

A diagnosis of Bouveret's syndrome should be considered in all patients with a history of gallstones and gastric outlet obstruction.

REFERENCES

1. Frattaroli F M, Reggio D, Guadalaxara A, Illomei G, Lomanto D, Pappalardo G. Bouveret's syndrome: case report and review of the literature. *Hepato-Gastroenterology* 1997; **44**: 1019-22.
2. Holl J, Sackmann M, Hoffman R, Schüssler P, Sauerbruch T, Jüngst D, Paumgartner G. Shockwave therapy of gastric outlet syndrome caused by a gallstone. *Gastroenterology* 1989; **97**: 472-4.
3. Rodriguez Romano D, Moreno Gonzalez E, Jimenez Romero C *et al.* Duodenal obstruction by gallstones (Bouveret's syndrome). presentation of a new case and literature review. *Hepato-Gastroenterology* 1997; **44**: 1351-5.

The Ulster Medical Journal, Volume 69, No. 1, pp. 71-73, May 2000.

Case Report

Neonatal diabetes mellitus

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Accepted 14 February 2000

Diabetes mellitus has many forms. Neonatal diabetes mellitus is one of the rarest, with a reported incidence of 1 in 450,000 live births.[1,2] The first case was described by Kitselle (1852) in his own newborn son, who subsequently died.[3] In Northern Ireland, one case might be expected approximately every 16 years; the last documented here was born in 1983.[4] Several literature reviews have highlighted the characteristic clinical picture of this disease.

Neonatal diabetes mellitus is defined as persistent hyperglycaemia within the first six weeks of life, requiring insulin for two or more weeks, in infants of 37 or more weeks gestation.[2,5] Alternative names are temporary idiopathic neonatal hyperglycaemia, neonatal pseudodiabetes mellitus, transient diabetes of early infancy and congenital temporary diabetes mellitus.[5,6] Neonatal diabetes differs from insulin-dependent (type I) diabetes in that it has a highly variable course. Some patients have permanent diabetes, while others have transient or lasting remissions. We report the latest case from Belfast.

CASE REPORT A male infant was admitted to the Royal Belfast Hospital for Sick Children in April 1998, aged six weeks. He was the first child of unrelated parents. His mother suffered from systemic lupus erythematosus and was treated with prednisolone 10 mg daily throughout the pregnancy. She had an uneventful antenatal course, but had proteinuria and mild hypertension at term. She had a normal delivery at 37 weeks of a male infant weighing 2.27 kg (2nd centile). He was well at birth and on account of the maternal history of systemic lupus erythematosus and increased risk of congenital heart block, he had an electrocardiograph before discharge, which was normal.

He fed eagerly and always appeared hungry. His parents contacted the health visitor as he was drinking excessive quantities of formula milk (3 oz every two hours, equivalent to 265 mls/kg/day). He had no vomiting or diarrhoea, but was not gaining weight. Two days prior to admission, he became very irritable and had some loose motions. His colour became grey and mottled. On admission he was profoundly dehydrated with a depressed fontanelle; his eyes were alert but he was very agitated. He was extremely restless and appeared emaciated, with tachycardia (200/min), tachypnoea (65/min) and fever of 38°C. He showed an unusually high level of consciousness for such a severely dehydrated infant. A ketotic smell was evident. He passed large volumes of dilute urine; urinalysis showed glucose ++++, protein ++, blood + and strongly positive ketones. Blood gas analysis showed marked metabolic acidosis (pH 7.162, pO_2 15.0 kPa, pCO_2 1.41 kPa, HCO_3 3.7 mmol/1 and Base excess – 22.7 mmol/l). Biochemical parameters were in keeping with the clinical signs of dehydration and severe hyperglycaemia (serum glucose 73.2 mmol/l, Na 154 mmol/1, K 5.8 mmol/l, Urea 15.1 mmol/1, Creatinine 62 umol/1, Hb 10.7 g/dL, WCC 19.4 x 10^3/ug, platelets 737 x 10^3/ug).

Initial management was with plasma volume expansion with human plasma protein fraction and saline, total volume 40 ml/kg, and intravenous insulin infusion. During rehydration he developed poor peripheral perfusion with oxygen desaturation, opisthotonus and seizure activity. He was transferred to the paediatric intensive care unit and was sedated, mechanically ventilated

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for three days and treated with anticonvulsants. His blood glucose levels fell slowly with repeated insulin injections. He resumed oral feeds and remained an inpatient for 24 days to establish the insulin and feeding pattern. By the age of 10 weeks his weight had increased to the 25th centile (5.16 kg).

A 14 months his developmental milestones were all normal. He remained on twice-daily subcutaneous medium-acting insulin. Home blood sugars were monitored daily and he had no apparent episodes of hypoglycaemia. HbA_{1c} concentration was 7.1% at age 16 months. To date there has been no evidence of remission and it is probable that diabetes will be a long-term problem.

DISCUSSION

Only 0.5% of children with diabetes develop the disease during the first year of life.[5] The incidence of newly diagnosed type I diabetes mellitus in Northern Ireland is 19.6 per 100,000 children under 15 years, and 18% of cases are under five years at diagnosis.[7] Long term studies of neonatal diabetes world-wide have shown that approximately 42% have permanent diabetes and 58% have a period of remission, with 65% of the transient forms subsequently becoming diabetic again.[2] Infants with the transient form usually become euglycaemic without insulin treatment within the first year.[8]

Babies with neonatal diabetes are usually small for dates term infants, as found in the case presented. In one study, 41 out of 45 babies (91%) had low birth weight (<2nd centile).[2] They develop hyperglycaemia with severe dehydration and minimal ketosis. Seventy-five percent of cases first present with symptoms within 10 days of birth.[5] The picture of a lively, alert but grossly dehydrated child is classical, in contrast to the semicomatose state and glazed-eye appearance usual in severely dehydrated infants.[3,6] Polyuria is difficult to recognise in the newborn.

With few exceptions, most infants require exogenous insulin. Total daily doses of 0.2-1.0 units/kg are usually sufficient to establish normoglycaemia, and mild hyperglycaemic values are well tolerated. Hypoglycaemia is the greatest complication of insulin therapy, with associated risk of cerebral damage.[3,6,9] Small, intermittent doses of regular insulin, along with frequent blood sugar monitoring has been advised to avoid hypoglycaemia.[10] After initiation of insulin therapy, weight gain usually accelerates.[3,5]

The frequency of relapse in children with transient neonatal diabetes is difficult to define. One study showed a median duration of exogenous insulin requirement of three months,[1] and another showed a mean insulin requirement of 120 days;[2] and a period of remission until later recurrence of diabetes of 7-20 years (median 13 years).[2] Long term follow-up of the later onset diabetes is not the classical autoimmune related type I form of childhood, but is consistent with type II diabetes with insulin resistance.[1,8]

Various suggestions as to the pathogenesis of this condition have been proposed, including reduced insulin production from pancreatic dysmaturity,[11] insulin resistance[8,9] and insulinopenia from a poor response of the pancreatic beta cell to hyperglycaemia.[5] The onset of islet cell damage or destruction is thought to start in utero, as poor insulin secretion by the pancreas has been quantified by low levels of C-peptide in the neonatal period.[4,12] The fact that most babies are low birth weight may be related to the lack of the anabolic effect of insulin, as insulin is one of the main growth factors in-utero.[1,12] The autoimmune theory of classical juvenile type I insulin dependent diabetes is not applicable to neonatal diabetes, as there has been no evidence of islet cell antibodies developing.[1,2,5] Heredity plays an important role as approximately 25% of neonatal cases have an affected sibling (with type I insulin dependent diabetes), with equal sex ratios.[5,6] Minorities of patients have shown HLA haplotypes typical for insulin-dependent diabetes (HLA DR3 and DR4).[2]

Recently, the genetic basis of neonatal diabetes has been studied. Shield et al showed on molecular DNA analysis paternal uniparental disomy of chromosome 6 in many cases with the temporary form of neonatal diabetes.[1,11,13] This refers to the inheritance of both chromosomes of one pair from one parent only, with no contribution from the other. The findings predict that neonatal diabetes is due to the overexpression of an imprinted gene at 6q22-23,[1,13,14] and this gene may prove to be an important factor in the aetiology of more common types of adult diabetes.[14] Hermann et al suggested that the two phenotypes of transient and permanent neonatal diabetes have different genetic backgrounds, as none of the cases with permanent neonatal diabetes

have shown the paternal uniparental disomy of chromosome 6.[15]

Several associations of neonatal diabetes with other developmental or dysmorphic syndromes have been described. Ten cases have been reported of the Wolcott-Rallinson syndrome (a rare autosomal recessive condition characterised by diabetes mellitus in early infancy and multiple epiphyseal dysplasia) all of whom have had permanent diabetes, and a high risk of early mortality from renal impairment.[2, 16] Two cases have been described of brothers with X-linked hyperuricaemia, secondary to phosphoribosyl-ATP pyrophosphatase hyperactivity who became diabetic within the first day of life, both had severe developmental delay.[2] Macroglossia has been reported in patients with transient neonatal diabetes, this feature becomes less pronounced with age.[1, 15]

The combination of systemic lupus erythematosus and pregnancy increases both fetal and maternal risks, with a reported 20-60% flare up of systemic lupus erythematosus, 23% early foetal loss, 50% pre-term delivery and 10% growth retardation.[17] The infants have an increased risk of congenital heart block, neonatal lupus and intra-uterine death. Systemic prednisolone 10 mg/day is well tolerated in planned systemic lupus erythematosus pregnancies.[17] We have found no previous reported cases of maternal systemic lupus erythematosus and neonatal diabetes mellitus, although one infant with initial hypoglycaemia, who was treated with steroids and subsequently developed hyperglycaemia requiring insulin, has been classified as "steroid-provoked" diabetes.[9]

The overall outcome for general health and normal intellectual development is usually good Complications of vasculopathy are rare in long-term follow up-reports over 20 years.[2, 5] The prognosis is worst in permanent diabetes with onset after one month of age, and in association with HLA DR3/DR4 halotypes, and the other rarer associated syndromes.[2]

REFERENCES

1. Shield J P H, Gardner R J, Wadsworth E K J, Whiteford M L, James R S, Robinson D O, Baum J D, Temple I K. Aetiopathology and genetic basis of neonatal diabetes. *Arch Dis Child* 1997; **76**: F39-F42.
2. Von Mühlendahl K E, Herkenhoff H. Long-term course of neonatal diabetes. *N Engl J Med* 1995; **333**: 704-8.
3. Hutchinson J, Keay A J, Kerr M M. Congenital temporary neonatal diabetes. *BMJ* 1962; **2**: 436-40.
4. Halliday H L, Reid M, Hadden D R. C-peptide levels in transient neonatal diabetes. *Diabet Med* 1986; **3**: 80-1.
5. Fosel S. Transient and permanent neonatal diabetes. *Eur J Pediatr* 1995; **154**: 944-8.
6. Lewis S R, Mortimer P E. Idiopathic neonatal hyperglycaemia. *Arch Dis Child* 1964, **39**: 618-24.
7. Patterson C C, Carson D C, Hadden D R. Epidemiology of childhood IDDM in Northern Ireland 1989-1 994: Low incidence in areas with highest population density and most household crowding. *Diabetologica* 1999; **39**: 1063-9.
8. Shield J P H, Baum J D. Transient neonatal diabetes and later onset diabetes: a case of inherited insulin resistance. *Arch Dis Child* 1995; **72**: 56-7.
9. Chance G W, Bower B D. Hypoglycaemia and temporary hyperglycaemia in infants of low birth weight for maturity. *Arch Dis Child* 1966; **41**: 279-85.
10. Mitamura R, Kimura H, MurakamiY, Nagaya K, Makita Y, Okuno A. Ultralente insulin treatment of transient neonatal diabetes mellitus. *J Pediatr* 1996; **128**: 268-70.
11. Milner R D G, Ferguson A W, Naidu S H. Aetiology of transient neonatal diabetes. *Arch Dis Child* 1971; **46**: 724-6.
12. Bappal B, Raghupathy P, de Silvia V, Al Kusaiby S M. Permanent neonatal diabetes mellitus: clinical presentation and epidemiology in Oman. *Arch Dis Child* 1999; **80**: F209-F21 2.
13. Gardner R J, Mungall A J, Dunham I, Barber J C, Shield J P H, Temple I K, Robinson D O. Localisation of a gene for transient neonatal diabetes mellitus to an 18.72 cR3000 (approximately 5.4 Mb) interval on chromosome 6q. *J Med Genet* 1999; **36**: 192-6.
14. Temple I K, Gardner R J, Robinson D O, Kibirige M S, Ferguson A W, Baum J D, Barber J C K, James R S, Shield J P H. Further evidence for an imprinted gene for neonatal diabetes localised to chromosome 6q22-q23. *Hum Mol Genet*, 1996; **5**: 1117-21.
15. Hermann R, Laine A P, Johansson C, Niederland T, Tokarska L, Dziatkowiak H, Ilonen J, Soltesz G. Transient but not permanent neonatal diabetes mellitus is associated with paternal uniparental isodisomy of chromosome 6. *Pediatrics* 2000; **105**: 49-52.
16. Stewart F J, Carson D J, Thomas P S, Humphreys M, Thornton C, Nevin N C. Wolcott-Rallinson syndrome associated with congenital malformations and a mosaic deletion 15q 11-12. *Clin Genet* 1996; **49**: 152-5.
17. Lê Thi Huong D, Wechsler B, Vauthier-Brouzes D, Seebacher J, Letébvre G, Blétry O, Darbois Y, Godeau P, Piette J C. Outcome of planned pregnancies in systemic lupus erythematosus: a prospective study on 62 pregnancies. *Br J Rheum* 1997; **36**: 772-7.

The Ulster Medical Journal, Volume 69, No. 1, pp. 74-75, May 2000.

Case Report

Ureteric kinking after colposuspension:
a case report and review of the literature

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Accepted January 2000

CASE REPORT A 40-year-old woman was referred by her general practitioner because of urinary incontinence that was getting worse on walking and exercising. In the past she had a vaginal hysterectomy and anterior colporraphy. In the clinic stress incontinence was demonstrated and in view of her previous anterior repair she was referred for urodynamic investigation. Uroflowmetry revealed a maximum flow rate of 10 ml per second for a voided volume of 225 ml, and cystometry revealed a stable detrusor and genuine stress incontinence.

The patient chose to have surgical treatment, as she was getting no benefit from physiotherapy. She was advised about the possibility of voiding difficulty after bladder-neck surgery, which might require the use of intermittent clean self-catheterisation. In anticipation of this complication the continence adviser nurse taught her the technique of intermittent clean self-catheterisation.

Burch's colposuspension was performed uneventfully in March 1998 with development of the retropubic space of Retzius, identification of the urethrovesical angle and the vaginal cone on either side as usual. Two Ethibond sutures were inserted in the vagina lateral to the urethrovesical angle and hitched to the ipsilateral ileopectineal ligament. A Redivac drain was left in the retropubic space of Retzius and a supra-pubic catheter was inserted into the bladder.

On the first post operative day urine output was decreased and concentrated, but responded to an intravenous fluid load. Later in the day she had nausea and vomiting. On the fourth postoperative day she complained of severe backache and had mild pyrexia of 37.8 C. On examination there was tenderness over the right renal angle. Ultrasound examination showed right-sided hydronephrosis. Intravenous urography confirmed hydronephrosis and also showed incomplete filling of the right ureter. The patient was taken back to theatre and the abdomen was reopened to the cave of Retzius. The two sutures on the right ileopectineal ligament were identified, released from the ligament and removed from the vaginal fascia. The patient was immediately pain free after she recovered from anaesthesia and a repeat intravenous urography two days later revealed a patent right ureter and resolving dilatation of the right renal pelvis.

The patient was reviewed in the clinic two months later. She maintained her improvement and she was continent of urine. On vaginal examination the urethra was well supported close to the under-surface of the pubic symphysis and the urethrovesical angle well elevated.

COMMENT

Despite the widespread use of Burch's colposuspension in the surgical management of genuine stress incontinence, only eight reports of ureteric kinking after colposuspension have been published comprising a total of 23 cases. Since the ureter has a firm fibromuscular coat, vaginal elevation from sutures placed well away from its course are not likely to cause kinking or obstruction. Previous surgery causes fibrosis and

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scarring of the local tissues, thereby increasing the potential for ureteric kinking and or damage during colposuspension. Particular care should be taken with the placement of the sutures into the vagina when the dissection is complicated by previous surgery causing retro-pubic fibrosis, genital prolapse, concomitant hysterectomy or haemorrhage from the venous plexus around the endo-pelvic fascia and the arcus tendineous fascia pelvis.[1]

Previous surgery has been a major predisposing factor for ureteric injury in published reports. In the current case the patient had previous vaginal hysterectomy and anterior repair. Rosen *et al* [1] reported 4 cases of ureteric injury after colposuspension. Two patients had had previous caesarean sections, one had had a previous abdominal hysterectomy and Marshal Marchetti Krantz vesico-urethropexy and one had had a previous hysterectomy and vaginal repair. Kinn and Sjoberg[2] reported two cases of bilateral ureteric kinking following colposuspension. One patient had had abdominal hysterectomy and the other patient had had anterior repair and urethropexy.

In this case the ureteric kinking was unilateral, while in the 23 cases in the literature 15 were unilateral and eight were bilateral. The average time for diagnosis of the obstructive uropathy in the literature was 3.3 days (range 1-9 days). Depending on whether the obstruction was unilateral or bilateral the clinical presentation included a combination of anuria, persistent fever and loin pain.

The complication has been managed in various ways, all of which appear to have been successful. In the current case removal of the colposuspension sutures on the affected side promptly relieved the kinking with resolution of all symptoms. Other methods have included ureteric stenting, cystoscopic removal of the offending suture[3] and percutaneous nephrostomy.[4] Other treatments have involved uretro-neocystostomy with anti-reflux tunnelling.[1]

Percutaneous nephrostomy has several advantages. It helps to identify the site of obstruction, and allows antegrade stenting from the renal pelvis. It also preserves renal function allowing the patient to stabilise and local tissue oedema to reduce so that the affected ureter may open spontaneously.[1]

Although ureteric kinking is a devastating complication of colposuspension it is fortunately rare, and the main long-term complications remain: de novo detrusor instability (14.7%), voiding difficulty (22%) and recurrent urinary tract infection (4.6%).[5]

REFERENCES

1. Rosen D M, Korda A R, Waugh R C. Ureteric injury at Burch colposuspension. 4 case reports and literature review. *Aust NZ J Obstet Gynecol* 1996; **36**: 354- 8.
2. Kinn A C, Sjöberg B. Anuria complicating urethrocystopexy. *Acta Obstet Gynecol Scand* 1985; **64**: 283-5.
3. Ferrani R A, Silva de Sai M F, Dias de Moura M, Charaffeding M N, Hockgreb de Freitas Junior A. Ureteral blockage as a complication of Burch colposuspension: report of 6 cases *Gynaecol Obstet Invest* 1990; **29**: 239-40.
4. Virtanen H S, Kiilholma P J A, Nurmi M J, Chancellor M B. Ureteral injuries in conjunction with Burch colposuspension. *Int Urogynaecol* 1995; **6**: 114-8.
5. Alcalay M, Monga A, Stanton S L. Burch colposuspension: a 10-20 year follow up. *Br J Obstet Gynaecol* 1995; **102**: 740-5.

The Ulster Medical Journal, Volume 69, No. 1, pp. 76-80, May 2000.

Association of Clinical Pathologists Irish Branch: Autumn Meeting 12 and 13 November 1999, Craigavon

MOLECULAR DIAGNOSIS OF AETIOLOGICAL AGENTS OF CULTURE-NEGATIVE MENINGITIS

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Rapid and accurate diagnosis is crucial for effective treatment of bacterial meningitis. Bacteriological culture of cerebrospinal fluid (CSF) and blood is still the single most important laboratory investigation which is carried out. However, in some cases, bacteriological culture is unable to detect any causative organisms. This may be due to a number of reasons such as prior antibiotic therapy or, the causative agent may be extremely fastidious.

In this study, we investigated 400 culture-negative CSF samples from patients with suspected acute meningitis by employing 16S rRNA genes, as targets for DNA amplification technologies using the polymerase chain reaction (PCR). Five methods for DNA extraction were compared and the Qiagen Blood Kit proved to be the most reliable and effective. Using a eubacteria PCR method based on the amplification of a 216bp fragment of the 16S rRNA gene, all CSF samples were screened. Contamination was strictly controlled during DNA extraction and PCR amplification in order to avoid false positives. PCR products were sequenced using cycle sequencing on a 373 Applied Biosystems Sequencer.

After PCR amplification, 130/400 (33.5%) were positive. Forty six PCR products subsequently sequenced suggested the presence of DNA from the following: 2/46 *Propionibacterium* spp. (4.34%); 3/46 *Acinetobacter* spp (6.52%); 2/46 *Klebsiella pneumoniae* (4.34%); 2/46 *E. coli* (4.34%); 3/46 *Staphylococcus* spp (6.52%); 3/46 *Haemophilus influenzae* (6.52%); 7/46 *Neisseria meningitidis* (15.22%); 1/46 *Burkholderia* spp (2.17%); 10/46 unidentified bacterium and 14/46 mixed (30.43%).

In conclusion, such molecular based technologies may be used to ascertain the identity of the causal agents of culture-negative meningitis thereby leading to the earlier administration of appropriate chemotherapy to the patient and to ascertain the need for prophylaxis and vaccination of contact cases.

(This work was supported by the Meningitis Research Foundation)

FATAL PULMONARY EMBOLISM IN A TEENAGE GIRL: A CASE REPORT

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A 19 year old female student was unwell for one week with symptoms of a respiratory tract illness. While being seen by General Practitioner she developed cardiorespiratory arrest. Attempts at resuscitation were unsuccessful. Post-mortem examination revealed bilateral pulmonary thromboemboli and pulmonary infarction with free and organised thrombus of the pelvic veins. Histology showed inflammatory myocardial changes which are discussed. Risk factors for thrombus formation such as smoking or obesity were not present. The only risk factor for thromboembolism identified was oral contraceptive use. Studies have shown that oral contraceptives increase the incidence of venous thrombosis and embolism three to four fold. This is presumed to result from their effects on the haemostatic system. Increased activity of coagulation factors, enhanced platelet activity and a reduction in antithrombin III levels have all

been observed with pill usage. An inherited thrombophilic disorder is not uncommonly found among patients with venous thrombosis, and in oral contraceptive users may increase the risk of thrombosis as much as thirty to fifty fold. A thrombophilia screen of family members undertaken revealed a slightly prolonged activated partial thromboplastin time in female family members with no inhibitor present. Further studies showed a reduction in factor XII levels below the normal range. Otherwise the thrombophilia screen was normal. We conclude that mild reduction of Factor XII levels may constitute a previously unrecognised risk factor for thrombembolic disease in contraceptive pill users.

PCR DETECTION OF FUNGAL AGENTS IN THE IMMUNOCOMPROMISED AND IMMUNOCOMPETENT HOST

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Laboratory culture and serological methods continue to be the diagnostic cornerstone in the detection of medically important fungi in a variety of disease states, including endocarditis, meningitis, febrile neutropenia, diabetes, cystic fibrosis. However fungi are difficult to culture *in vitro* and therefore present diagnostic problems under such circumstances. Employment of the nuclear rDNA genes encoding the 5S, 18S, 5.8S and 28S rRNA offers a molecular basis for both the detection and the identification of fungi.

The aim of this study was (i) to ascertain a suitable method to extract yeast/fungal DNA from various fluid and tissue samples from patients with suspected fungal infections, (ii) to detect and identify these microbiological agents by amplification of various ribosomal target gene loci i.e. small ribosomal subunit (18S rRNA), large ribosomal subunit (28S rRNA), 5.8S rRNA and interspacer regions ITS1 and ITS2, using PCR and direct sequence analysis, (iii) to separate and identify multiple fungal agents in a single clinical specimen.

Twenty five medically important fungi were analysed by PCR amplification and sequence analysis in order to ascertain that the ITS region was the most suitable for detection and accurate identification.

The optimum method demonstrated included an initial DNA extraction method comprising treatment of the specimen with lyticase followed by extraction with proteinase K, guanidine hydrochloride. It was noted that care should be taken in extracting BacTAlert blood culture material, as it was shown that this material was intrinsically contaminated with DNA from both *Lactococcus lactis* and *Saccharomyces cerevisiae*. Primer selection indicated was the ITS1 and ITS2 regions for detection and the 5.8S – ITS2 region for sequence identification. Where sputa are shown to contain several mixed fungal genera and species, it is recommended that each species be separated on a high-resolving acrylamide gel (ExcelGel 48S, Pharmacia), before excision and simple elusion, reamplification and sequence analysis of single clones.

In conclusion, this optimised method may allow for a better understanding of fungi in infection and help in deciding the most appropriate management of the patient.

This work was supported by the Action Cancer, the British Heart Foundation, the Meningitis Research Foundation, the Primary Immunodeficiency Association and the Cancer Research Campaign.

ERYTHROPOIETIN RESPONSE TO TRAUMA

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Erythropoietin (EPO) is essential for the production of red blood cells. However in a number of conditions the normal relationship between anaemia, hypoxia and EPO production is not so clearly defined and EPO response may be inhibited. The aim of this study was to investigate the EPO response to trauma, and its variation with time and degree of injury.

Eighteen trauma patients admitted to The Intensive Care Unit of The Royal Victoria Hospital were studied. All had an Injury Severity Score (ISS) ≥16, and were enrolled within 16 hours of injury. Blood samples were taken every

four hours for 24 hours, every eight hours for the next 48 hours and daily thereafter until day 7. The samples were spun, aliquoted and frozen to – 70°C within one hour of sampling for subsequent EPO, Interleukin-6 (Il-6) and soluble tumour necrosis factor receptor – p55-measurements.

Two patient groups were defined with ISS scores 25 and 25 respectively and were otherwise well matched.

Both levels of injury severity resulted in significantly elevated levels of erythropoietin ($p<0.05$). The more severely injured group had an initially higher level of EPO, with the less severely injured reaching this level within 24 hours. The median concentration of EPO in either group did not reach a therapeutic range at any time. Both groups demonstrated significantly elevated levels of both p55 and IL-6, with no significant difference between ISS groups. The three patients who died from multiple organ dysfunction (MODS), revealed initial elevated EPO levels which were significantly higher than the levels seen in those patients who survived. This initially high EPO concentration decreased towards normal within 24 hours. In conclusion trauma appeared to blunt the normal EPO response; however there was no correlation with degree of injury.

ADVERSE HISTOPATHOLOGICAL FEATURES IN CERVICAL LESIONS AS PREDICTORS OF HIGH RISK HUMAN PAPILLOMA VIRUS INFECTION

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Human Papilloma Virus (HPV), which is the main aetiological agent in cervical cancer has been found to induce a number of cytopathic effects in cervical squamous cells. Koilocytic change has long been recognised as an indicator of low risk HPV infection in pre-malignant and malignant lesions. We examined a number of histopathological features and their relationship with high risk HPV infection.

DNA was extracted from a total of 83 microdissected archival cervical lesions using single step proteinase K digestion. The HPV status of the lesions was determined by PCR using generic primers for HPV types 16, 18, 31, 33, 52, 58, 6 and 11 and type specific primers for HPV 16 and 18. HPV PCR products were confirmed by restriction enzyme digestion. Haematoxylin and eosin stained sections were reviewed for the presence of six histopathological features some of which have been previously shown to be associated with microinvasive cancer. Bivariate analysis was used to determine the relationship between the presence of adverse histopathological features and infection with HPV 16 and 31.

All of the histopathological features examined were shown to have a strong statistical relationship with grade of lesion. Absence of koilocytic change was a feature of high grade and invasive lesions. Statistical significance was found between infection with HPV 16 and 31 and all of the histopathological features.

The absence of koilocytic change and the identification of histopathological markers particularly intralesional squamous maturation, comedo necrosis and apoptosis in cervical lesions should be seen as indicators of the presence of high risk HPV types and therefore a potential for progression.

PYREXIA OF UNKNOWN ORIGIN

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Pyrexia of unknown origin remains a common diagnostic challenge for both the clinician and histopathologist. We report the case of an elderly female patient admitted to a district general hospital with rectal bleeding due to over anticoagulation with warfarin. She had many medical problems and described a six month history of nausea, weight-loss, lethargy and sweats. As an-inpatient she had persistent pyrexia despite antibiotic cover. Extensive investigations failed to establish a diagnosis and a bone marrow aspirate and trephine biopsy were performed. A subsequent Ziehl-Neelsen stain on sections of the trephine biopsy revealed the presence of acid-fast bacilli. Anti-tuberculous therapy was instituted and her pyrexia settled over a four week period. Unfortunately she later succumbed to cardiac and renal failure. *Mycobacterium tuberculosis* remains the leading cause of mortality worldwide with three million deaths per year, many cases being diagnosed at autopsy.

Bone marrow examination remains a most useful investigation in patients with pyrexia of unknown origin.

CORRELATION OF DNA PLOIDY, GRADE AND OTHER PROGNOSTIC PARAMETERS IN 156 CASES OF BREAST CARCTNOMA

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We present a retrospective study of 156 patients with breast cancer and correlate the following parameters: ploidy, histological type, histological grade, estrogen receptor, lymph node status, and tumour size.

All the data was collected from the Department of Histopathology at University College Hospital, Galway, between 1996 and early 19999. 83 cases showed a DNA diploid pattern (53.2%) and 73 cases showed a DNA aneuploid pattern (46.7%).

We found a strong correlation between ploidy and the histological grade of the tumour ($p<0.001$). However, no correlation was found between ploidy and the other parameters.

RHABDOMYOSARCOMA MIMICKING AN ACUTE HAEMATOLOGICAL MALIGNANCY

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A previously fit 17-year-old male was admitted feeling generally unwell with a purpuric rash. Examination revealed sternal tenderness, hepatomegaly and a right pleural effusion. Initial investigations confirmed thrombocytopenia (19 x 10^9/l) with an otherwise normal blood count. Hypercalcaemia (2.87 mmol/1), elevated liver function tests and a markedly raised LDH level (5166 u/1) were also found.

Peripheral blood film inspection showed the presence of blasts and nucleated red cells while clumps of small round cells were demonstrated on pleural fluid aspiration. A bone marrow biopsy was carried out to confirm our suspicion of acute leukaemia. Aspirate showed clumps of abnormal cells, and examination revealed a solidly hypercellular core packed with small round cells. LCA, CD3 and CD79a markers were negative disproving our primary diagnosis. CAM 5.2 chromogranin, NSE + MIC2 stains were also negative although the Desmin stain was strongly positive giving a diagnosis of rhabdomyosarcoma.

His condition deteriorated due to disseminated intra vascular coagulation and a right haemothorax, despite treatment with IV ifosphamide, doxorubicin, and hydrocortisone. A thoracotomy was required and multiple pleural and pericardial tumour deposits were noted along with a soft tissue mass arising from the chest wall. He died two weeks from presentation.

Extensive marrow infiltration by rhabdomyosarcoma is a rare phenomenon presenting like an acute leukaemia in a handful of reported cases. The differential diagnosis of small round cell tumours includes leukaemia/ lymphoma, peripheral neuroectodermal tumours (PNETS), Ewing's or other sarcomas and neuroblastomas. This case illustrates the need for marker studies to enable a correct diagnosis of these aggressive tumours to be reached.

GRANULOCYTIC SARCOMA PRECEDING A DIAGNOSIS OF ACUTE MYCLOID LEUKAEMIA (M0)

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In July 1998, a previously fit and well 35-year-old male presented to a local hospital with bilateral inguinal lymphadenopathy. He was otherwise asymptomatic with no sweats or weight loss. Biopsy of an excised node showed complete effacement of the normal lymph node architecture with a diffuse infiltrate of large cells. The appearances were felt to be in keeping with a T-cell Non-Hodgkins Lymphoma. A staging CT scan revealed a small group of nodes in the para-aortic and iliac areas; full blood picture and bone marrow biopsy were normal. The patient was commenced on standard 'CHOP' chemotherapy and CT scanning following the third cycle of CHOP showed shrinkage of all nodes to <1 cm. The patient completed 6 cycles of CHOP and was placed on regular review thereafter.

In April 1999, one month post final chemotherapy cycle, the patient complained of night sweats and again swelling in the inguinal area. Further biopsy of an inguinal node again showed total effacement

of the nodal architecture with lymphoid cells, negative for B-cell markers, but focally positive for CD3. It was felt the features were similar to the previous biopsy and again peripheral T-cell lymphoma was diagnosed. The patient was referred to Belfast City Hospital for salvage therapy.

On admission, a full blood picture revealed the patient to be leucopenic with 13% 'blasts' in the peripheral blood. An immediate bone marrow biopsy was performed and this revealed that 84% of the aspirate consisted of blasts. Immunophenotyping showed the blasts to be Sudan black & ANAE negative, but positive for TdT, LCA, HLA-Dr, CD34 and CD33. It was felt this represented an AML M0, preceded by a granulocytic sarcoma which had been mix-diagnosed as Non-Hodgkins Lymphoma. This was confirmed by further staining of the original lymph nodes – now found to be positive for TdT and CD34.

This case is unusual in that development of AML M0 was preceded by a granulocytic sarcoma 9 months previously. It illustrates the pathological pit-falls in the diagnosis of this difficult condition when it occurs without concomitant blood disease. To our knowledge, this is only the second case of granulocytic sarcoma preceding AML M0 to be reported.

MOLECULAR STUDIES IN LYMPHOID MALIGNANCIES

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Immunophenotyping is essential in the study of chronic lymphoproliferative disorders (CLPD) and has led to improved classification and to more effective treatment. Cytogenetic and molecular studies offer a similar ability to define subcategories but are not widely applied.

PCR may be used to demonstrate immunoglobulin heavy chain (IgH) and T-cell receptor (TCR) gene rearrangements. IgH and TCR are coded by several different gene segments which in the germline are widely separated, but become juxtaposed during rearrangement allowing the amplification of a region by PCR. IgH and TCR rearrangements represent unique clonal markers and their study may therefore be used to assess clonality in lymphoid malignancies. Primers have been designed and methods established for the detection of clonal TCRß (partial and complete), TCRγ and IgH (frameworks 3, 2a and 2b) gene rearrangements.

Similar methods have been established for detection of chromosomal translocations commonly found in subcategories of CLPD including t(14;18), t(8;14), t(11;14) and t(2;5). These molecular methods have the potential to make a major contribution in the diagnosis of follicle centre NHL, Burkitt's NHL, mantle cell NHL and anaplastic large cell lymphomas, respectively.

These methods are equally applicable to the study of DNA extracted from peripheral blood or bone marrow cells, bone marrow trephines or formaldehyde-fixed, paraffin wax embedded tissue biopsies. They can be used to confirm clonality, although unlike immunophenotyping are not lineage specific.

Additionally, with advances in the treatment of patients with chronic lymphoid malignancies, they will have an increasing role in the detection of minimal residual disease post-treatment and in the detection of residual tumour in peripheral blood stem cell harvests. Used in conjunction with conventional techniques such as morphology, cytochemistry and immunophenotyping they can provide clinically relevant diagnostic and prognostic information and could lead to proposals for MIC-M classifications of chronic lymphoid malignancies.

The Ulster Medical Journal, Volume 69, No. 1, pp. 81-82, May 2000

Book Reviews

Quality Assurance in Dialysis. 2nd Edition. Edited by Lee W Henderson and Richard S Thuma. Kluwer Academic Publishers; ISBN 0792352815; pp 301; £92.

Quality assurance is the hot issue in nepbrology. In the 1980s attention was drawn to the importance of ensuring an adequate delivered dose of haemodialysis by data from the National Cooperative Dialysis Study in the United States, showing an inverse link between mortality and the amount of solute removed at each dialysis session. A growing awareness of quality, along with innovations such as erythropoietin therapy, has led to maintenance dialysis becoming a technique for enhancing rather than merely prolonging life. In the United Kingdom, the standards document of the Renal Association has defined a set of quality guidelines, rated according to best evidence, and the Renal Registry will enable units to monitor their performance in comparison to their peers. The nephrology group of the Cochrane Collaboration will help to define evidence for quality recommendations, although controlled trials in dialysis medicine remain rare. This whole area has assumed even more importance with the introduction of clinical governance.

This edition is an update of a title first published in 1994. The viewpoint is that of a commercial dialysis concern in the US and the editors and many chapter authors are associated with Baxter Healthcare Corporation. Nevertheless most of the topics are pertinent to the clinical practice of dialysis medicine in Europe.

At first glance it is not easy to discern the overall structure of the book. The preface does not make things much clearer. There are 26 individual chapters, not organised into sections. Broadly, the first ten chapters are mainly concerned with the methodology of defining and monitoring quality standards, including discussions of evidence based medicine, statistical methods, and outcome measures. The remaining chapters are directed more towards clinical practice. There are loose sections on predialysis patients, maintenance haemodialysis (including chapters on quality of life, selection of adequacy measures, dialysis water treatment and dialyzer reuse) and peritoneal dialysis, as well as two brief chapters on acute renal failure and renal transplantation.

It is a pity that, given the central theme of quality assurance, more attention has not been paid to the quality of language. The standard of the subediting is poor. There are many typographical errors, misspellings (*tendancy for tendency*) and malapropisms (*tenant for tenet*). Sentences are lengthy and unwieldy and full of jargon phrases. Frank errors of grammar and syntax are disappointingly common with verbs of incorrect number especially frequent. Some chapter titles are almost impossible to understand and some are ambiguous (despite first impressions, *Quality of Life Assurance in Hemodialysis* has nothing to do with what you get for the premiums paid to an insurance company). Sticklers may also wince at the frequent equivocal but a avoidable misdemeanours of style (split infinitives, small numbers appearing in the text as ciphers rather than words, singular verbs with Latin neuter plural subjects).

Although several of the chapters transcend these criticisms, there is a need for a better organised and better written book on this subject. In the meantime, despite its indigestibility, this volume will be essential reading for any renal physician with an interest in clinical governance; that is, every practising nephrologist.

P J GARRETT

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A major and often unsubstantiated criticism of the use of immortal cell lines in cancer research is that they are unrepresentative of the tumour from which they were derived. It is to the credit of the authors and editors that these criticisms are dealt with, primarily by emphasising the similarity in histopathology and molecular genetics of the tumour cell lines and the clinical specimens from which they were derived. A particularly important chapter in this regard compares a large series of new breast cancer cell lines with the corresponding tumour and shows that cell lines retain many phenotypic and genotypic features of the corresponding tumour for long periods of time.

This volume represents an excellent addition to an important series and can be recommended to post-graduates, post-doctoral fellows, MD students or clinicians considering using human tumour cell lines as experimental models.

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The Ulster Medical Journal, Volume 69, No. 1, pp. 81-82, May 2000

Book Reviews

Quality Assurance in Dialysis. 2nd Edition. Edited by Lee W Henderson and Richard S Thuma. Kluwer Academic Publishers; ISBN 0792352815; pp 301; £92.

Quality assurance is the hot issue in nepbrology. In the 1980s attention was drawn to the importance of ensuring an adequate delivered dose of haemodialysis by data from the National Cooperative Dialysis Study in the United States, showing an inverse link between mortality and the amount of solute removed at each dialysis session. A growing awareness of quality, along with innovations such as erythropoietin therapy, has led to maintenance dialysis becoming a technique for enhancing rather than merely prolonging life. In the United Kingdom, the standards document of the Renal Association has defined a set of quality guidelines, rated according to best evidence, and the Renal Registry will enable units to monitor their performance in comparison to their peers. The nephrology group of the Cochrane Collaboration will help to define evidence for quality recommendations, although controlled trials in dialysis medicine remain rare. This whole area has assumed even more importance with the introduction of clinical governance.

This edition is an update of a title first published in 1994. The viewpoint is that of a commercial dialysis concern in the US and the editors and many chapter authors are associated with Baxter Healthcare Corporation. Nevertheless most of the topics are pertinent to the clinical practice of dialysis medicine in Europe.

At first glance it is not easy to discern the overall structure of the book. The preface does not make things much clearer. There are 26 individual chapters, not organised into sections. Broadly, the first ten chapters are mainly concerned with the methodology of defining and monitoring quality standards, including discussions of evidence based medicine, statistical methods, and outcome measures. The remaining chapters are directed more towards clinical practice. There are loose sections on predialysis patients, maintenance haemodialysis (including chapters on quality of life, selection of adequacy measures, dialysis water treatment and dialyzer reuse) and peritoneal dialysis, as well as two brief chapters on acute renal failure and renal transplantation.

It is a pity that, given the central theme of quality assurance, more attention has not been paid to the quality of language. The standard of the subediting is poor. There are many typographical errors, misspellings (*tendancy for tendency*) and malapropisms (*tenant for tenet*). Sentences are lengthy and unwieldy and full of jargon phrases. Frank errors of grammar and syntax are disappointingly common with verbs of incorrect number especially frequent. Some chapter titles are almost impossible to understand and some are ambiguous (despite first impressions, *Quality of Life Assurance in Hemodialysis* has nothing to do with what you get for the premiums paid to an insurance company). Sticklers may also wince at the frequent equivocal but a avoidable misdemeanours of style (split infinitives, small numbers appearing in the text as ciphers rather than words, singular verbs with Latin neuter plural subjects).

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It is divided into 4 sections with subjects on the modelling of anaesthetic action, the perioperative use of intravenous hypnotic agents, the state of the art of neuromuscular blockade and the use of opioids for perioperative analgesia.

The first section covers, in some detail, the mathematics of the biophase (effect) site of anaesthetic agents especially by the total intravenous technique. There is duplication of subject matter between authors but there is not too much and it helps understanding. This section is certainly aimed at readers interested in the research aspects of this topic.

The next section, however, is aimed much more at the general anaesthetist with six chapters about Total Intravenous Anaesthesia (TIVA). Pump design, closed loop control, the effects of opiates on Propofol dose, awareness and target control for sedation and in the ICU are all covered. Some of the chapters are very useful, others are fairly superficial. The chapter on awareness would have been much better with some diagrams to aid understanding.

The third section on neuromuscular blocking (NMB) agents is a useful collection of articles covering computer-controlled infusions, profiles of recently introduced agents, use of NMB in the elderly and those with neuromuscular disease and lastly their use in the ICU.

The last section is an excellent group covering the use of the new rapidly and short acting opiate, Remifentanil; its pharmacology, its use in theatre and ICU, for sedation and as an postoperative analgesic by target controlled infusion. This section finishes with a chapter on the role of serotonin in postoperative nausea and vomiting. It is interesting reading but, as with many parts of this book, it does not fit easily in this section.

This books target audience is wide-ranging; from the researcher to the general anaesthetist. A book most will dip in and out of. It is not a book for the individual library but certainly one for the hospital or departmental library especially at the price of £88.

These meetings received financial support from AstraZeneca, GlaxoWellcome and Organon with GlaxoWellcome providing funding support for this publication. This has had a bearing on the subject matter.

JULIAN R JOHNSTON

Fundamentals of Cardiovascular Pharmacology. G D Johnston. John Wiley & Sons. ISBN 0 471 97 13 1 Hardback £75. ISBN 0 471 85471 9. Paperback £34.95.

The main criticisms of textbooks are that they are long, boring, outdated and expensive. I am pleased to say Professor Johnston's book avoids all these traps. A book is usually interesting when, as is the case here, it is written by an acknowledged expert in the subject, who in this case can mix in depth knowledge of basic pharmacology with extensive clinical experience. The balance of what is or isn't important comes naturally. Being currently involved in the area also means that the book is as up to date as it can be, with references from 1998. Doubtless future revisions will keep it that way. As to expense, the hardback version may be a bit of a luxury, but the softback contains the same facts at half the price!

The way in which the text is laid out means there is bound to be some duplication. For instance, aspirin and digoxin are mentioned in several places, but not fully discussed in any one of them, so the best way is to use the Index (which is commendably thorough) to identify all the places where they are mentioned. Action potentials are described on p.7 under basic physiology, and again on p.197 under antiarrhythmic therapy. One section which did have a slight distortion of emphasis was in the area of lipid lowering medication. Bile acid sequestrants are now rarely used except as add-on treatment, and nicotinic acid (niacin) is not available in the UK except in small doses as a vitamin supplement, despite its widespread (and continued) use in the USA.

The basic physiology and pharmacology are described in sufficient detail to enable an understanding of the mode of action and the limitations of the various drugs. In future editions, I think it might be helpful to include a section on the heart as an endocrine organ (natriuretic peptides and metallopeptidase inhibitors), and also a description of the factors influencing peripheral vascular control – the balance of vasoconstrictor and vasodilator hormones and the role of EDRF/NO.

Overall I thought this was an excellent introduction to the subject with enough detail to keep postgraduates interested too. If it sells as well as the book by Professor Johnston's distinguished predecessor did, then perhaps we can look forward to a new university concert hall!

PAUL NICHOLLS

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