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BOOK REVIEW

A guide to radiological procedures. By Stephen Chapman and Richard Nakielny. 2nd ed. (pp 274. £8.95). London: Baillière Tindall, 1986.

It is a pleasure to recommend the second edition of this book. I can only repeat what I have said about the first edition — that it represents excellent value for money. I think the authors are to be congratulated on the content and presentation, and their bravery in publishing a book on techniques should not be under-estimated, as virtually every radiologist has an individual approach to each examination. It is extremely difficult for the young radiologist to assemble all the basic information required in radiological procedures and the authors have managed to present this material in a form which will be useful to both trainees and senior staff.

One must, however, enter some minor caveats. The fact that iron deficiency anaemia is not mentioned as an indication for barium enema examination is surprising. Many radiologists would not recommend puncture of the posterior wall of the femoral artery as being a routine part of the Seldinger technique, and I find it surprising that various contrast media are recommended by their trade rather than their generic names. Some of the examinations included are virtually obsolete, such as gynaecography, for demonstration of the ovaries, and Myodil meatography, for acoustic neuroma, but to balance this the inclusion of indications for computed tomography and nuclear magnetic resonance imaging is to be welcomed. Ultrasound techniques are outside the remit of this work.

All in all, this is an excellent book. Obviously, if it is used by trainees in the context of the requirements of their own departments, it will prove to be of great value. It can be, therefore, highly recommended.

EMMcI

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THE ULSTER MEDICAL SOCIETY

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Medical ethics

Presidential address given to the Ulster Medical Society, 30 October 1986.

W G Irwin

The relevance of medical ethics to daily practice should be obvious to all doctors, but the relationship between 'ethics and practice' raises many complex moral issues. 'Medical ethics is not a new subject, but a vital aspect of all medical practice, the implications of which must be made explicit throughout medical education'.[1] The key word is 'explicit', because morality is a serious and abstract topic, even in medicine. Some doctors recoil from it, because of the jargon associated with it. Samuel Butler once said 'The foundations of morality are like other foundations; if you dig too much about them the superstructure will come tumbling down'. I will try therefore to be both explicit and short-lived, and will not dig too deeply into the moral foundations, just enough to prepare students and young doctors for moral decision-making.

The question may be asked sometimes, who should we blame but ourselves if we take wrong moral options? We should all like to shift the blame by shouting at and accusing someone else. That is not a feasible solution. My contribution is to try and express effectively an acceptable and practical framework of ethical principles which could provide a basis of moral reasoning in medical practice. The recently published report of an Institute of Medical Ethics Working Party on the teaching of medical ethics in British medical schools has found many deficiencies and made new recommendations for change.

Professional attitudes are often determined by ethical principles and moral values, which determine in our minds and conscience whether our actions are considered to be morally right or wrong.[2] By medical ethics I do *not* mean standards of professional competence or conduct, but rather as Dunstan has defined 'the obligations of a moral nature which govern the practice of medicine'. The words 'ethics' and 'morals' are used interchangeably.

Philosophy is firstly about the critical evaluation of assumptions and arguments, and secondly about the clarification of concepts being evaluated. Naturally, I hesitate before plunging into the deep waters of philosophy and moral philosophy, not being properly trained to do so. In all its aspects, philosophy is a peculiar and at times ambiguous activity, which means different things to different people at different times and places. Doctors understandably do not take kindly to spending valuable time in abstract debate about the meaning and function of words and phrases. Yet it is necessary to do so, as rationality is common to science and philosophy. By definition moral philosophy is concerned with the critical study of morality. It examines the basic principles, norms and values which underlie moral judgements. Raphael believes that it is not practical in any real sense.[3] It cannot and does not tell us what we should do. We must decide that for ourselves. His advice is 'Do not expect moral philosophy to solve

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the practical problem of life or to be a crutch on which you can lean'. This might appear at first glance to be contrary to my hypothesis, but moral philosophy cannot exist in a vacuum. It must examine real life problems and in this context be used to assist doctors both to be effective clinically and to take correct moral options.

ETHICAL PRINCIPLES AND CODES OF BEHAVIOUR

In order better to understand the application of moral reasoning to practical issues, I start with a summary of general ethical principles, doctrines and specific codes of behaviour, which teaching experience has shown to be essential learning, before proceeding to consider case examples. The Hippocratic Oath was probably written in the 5th century B.C. A doctor who takes the Oath swears above all to try to benefit his patient and especially not to harm him or her. He also swears never to divulge what he sees or hears in the course of his profession. The Declaration of Geneva is the modern restatement of the oath drawn up in 1947 by the World Medical Association and amended in 1973 and 1983.[4] Other specific codes of ethics soon followed which are listed and described in the BMA *Handbook of medical ethics*: Sydney in 1968 defined the criteria of brain death; Oslo in 1970 discussed the criteria for therapeutic abortion; Tokyo in 1975 adopted guidelines for doctors concerned with torture and punishment; and Lisbon in 1981 discussed patient rights and confidentiality. All these codes provide abundant guidelines on specific issues, but they do not resolve adequately the conflict between the claims of the individual and the wider requirements of society.

The general principles so important in applied ethics are as follows:-

1. *Beneficence.* One should do good to the patient. This needs to be tempered by the next principle.
2. *Non-maleficence (Primum non nocere).* Above all, one should do no harm. This is more stringently enforced than the first principle.
3. *Respect for the authority of the patient.* A patient should be free to determine his own actions and give consent to the treatment offered. Essentially autonomy is the capacity of the patient to think, decide and act on the basis of such thought and decision, freely and independently and without 'let or hindrance'.[5] The duty of beneficence or 'doing good' has to be moderated by the duty of respect for autonomy.
4. *Truth.* The principle of telling the truth cannot be regarded as an absolute moral principle, but it is an ideal to be pursued to enhance trust and confidence. Ethical principles conflict at times in relation to truth-telling and it is sometimes necessary to deceive a patient for his own good. Generally speaking, however, deception conflicts with one's desires to preserve patient autonomy and a sound healthy relationship.
5. *Preservation of life.* Phillips and Dawson[6] argue that maintaining respect for life is not synonymous with preserving life at all costs. The principle of trying to preserve life by any means gives rise to many modern dilemmas.
6. *Justice.* The principle of justice refers to the fair distribution of scarce resources within society and in its application may conflict with one's absolute moral principles and duty to individual patients. A true believer in utilitarianism would argue that resources should be deployed to the most cost-effective techniques in which benefits are clear in relation to costs. The

fundamental paradox of health care is that medical advances so often breed further needs and increase further requirements for care.[7] The further life expectancy is extended, the greater becomes the pressure to allocate more resources to geriatric services. The ideal of trying to provide health care for all needs is laudable, but it is impossible for the Exchequer to meet all demands and some form of rationing of resources is inevitable.

7. *Confidentiality.* The principle of confidentiality between doctor and patient is venerated in the Hippocratic tradition. The nature of professional confidence varies according to the form of consultation or examination. The doctor is responsible to the patient for the security and confidentiality of the information given to him. Even after death a doctor must preserve secrecy on all he knows.

THE MAJOR CATEGORIES OF ETHICAL THEORIES

In America for some years past, persons concerned with ethical matters have plied their trade in hospitals and medical centres. Have they been doing anything useful, or what are they supposed to be doing? To answer these questions we come to examine and discuss the two major types of ethical theories.

Deontological theories of ethics are based on the 'rights and duties' of persons (*deon* is the Greek word for duty).[9] In this group the consequences of one's actions are not taken into account. Much theological dogma common to the great Christian religions expects absolute obedience to moral rules, for example, the Ten Commandments. The orthodox religious view is that all human beings are morally equivalent and have equal natural rights: a right to life, a right not to be killed, and a moral duty not to kill others. Others do not believe that people intrinsically possess absolute moral values and have inherent moral rights. These opposing views conflict in moral judgements of everyday events, so that sometimes what may appear on superficial examination to be utilitarian, may on closer inspection turn out to be absolutist, and vice versa. The great religions probably postulate that moral decision-making should often be taken out of the sole hands of doctors and clear guidelines should be laid down by the State having listened obediently to the spiritual and moral teaching authority of the Church on behalf of humanity.

The second category of major ethical theory is that of *utilitarianism.*[10] Put in its simplest Benthamite terms, it is about maximising happiness and pleasure and minimising misery, pain and suffering as a consequence of action taken. The theory was subsequently modified in the 19th Century by John Stuart Mill[8] to the moral concept of the 'greatest happiness for the greatest number'. It would be difficult to persuade people today that a human being's ability to feel pain and pleasure was the sole fundamental moral criterion by which to judge his actions. Mill saw the ultimate goal in life as an existence as free as possible from pain and misery, and as rich as possible in enjoyment, in quality and in quantity.

It is necessary to complete our conceptual framework by mentioning briefly several more doctrines:

Acts and omissions. A small minority of doctors might advocate voluntary euthanasia for patients who desired to die to end prolonged suffering. As Arthur Hugh Clough said, 'Thou shalt not kill, but need'st not strive officiously to keep alive'. The doctrine of 'acts and omissions' needs to be examined in this context. Is there a moral difference between the act of killing and a failure to act which leads subsequently to the death of a patient?

In 1981, members of Life instigated legal procedures against a Derbyshire paediatrician, Dr Leonard Arthur, accusing him of the murder of a new-born infant with Down's Syndrome rejected by his mother. Dr Arthur was acquitted although he had only prescribed dihydrocodeine and nursing care to relieve suffering.[11] He did not adopt any extraordinary means of resuscitation to keep the baby alive when it became gravely ill, because the parents did not wish it. He made a judgement based on clinical and compassionate grounds. This case posed many moral problems. All doctors would recoil from actively killing an infant for fear of the moral outcry and the legal consequences of being accused of infanticide. Many would, however, support Dr Arthur's actions.

A patient of mine, a man aged 92, who had enjoyed good health for over 90 years, was admitted to hospital with a refusal to eat much food for several weeks. He developed marked weight loss and became helpless, bedridden and dependent. Routine radiological and blood investigations revealed nothing abnormal and he continued downhill. It became apparent that he had lost the will to live and was in a state of terminal depression. Let us suppose he had a coronary thrombosis in the presence of the ward consultant, who decided not to intervene with the mobile care unit, and the patient subsequently died. Was this omission morally acceptable or should he have striven officiously to keep him alive by resuscitation?

Suppose instead the consultant had sent for the coronary care team and after some delay the old chap had been kept alive but unconscious on a mechanical ventilator. Fearing brain damage from anoxia the consultant orders the machine to be switched off and the patient dies.

Judged by the basic principles enunciated of beneficence and non-maleficence, the moral consequences of the omission in the first instance, and the commission in the second case, are the same. In utilitarian moral terms a patient with anoxic brain damage would not have obtained benefit by being kept alive as a vegetable. The moral position must, however, be based on more than these considerations. As Gillon says, 'there is little doubt that both the consequences of an action and the doctor's beliefs and intentions about what he is doing are relevant to moral assessment'.[11] The crucial issue underlying the 'acts and omissions' doctrine is therefore the understanding and intent with which the doctor acted. Had he withheld treatment in a younger adult, his omission would have been regarded as morally indefensible. It is generally agreed, however, that it should not be for the law to decide the criminality of one decision or the other. Clinicians should be free to take these difficult ethical decisions without becoming defensive and living in fear of being arrested.

Ordinary and extraordinary means. Linked to the above doctrine is that of 'ordinary and extraordinary means'. Pope Pius XII in 1957 applied this to answer moral questions about the use of mechanical ventilation in cases of brain death.[12] It was sufficient in serious illness, he said, to use only ordinary means to preserve life and health. This was obligatory in moral terms. The use of respirators was classified then as 'extraordinary means' and morally optional depending upon the special circumstances of the patient and the wishes of his family. So 'extraordinary means' may be defined as treatment which involves a great burden for the patient and/or next-of-kin. There would be no moral distinction, however, between ordinary and extraordinary means if it was in the patient's best interests to be kept alive.

Double effect. This doctrine is designed by theologians to ease moral decision-making in situations when intended good effects are likely to be nullified by unintended but foreseeable bad effects: for example, a doctor may administer medical treatment which is required to save the life of a pregnant woman even though this results in the death of the fetus, since the death of the fetus was not itself sought; a hysterectomy may have to be performed on a pregnant female who has an advanced cancer of the uterus.

APPLIED ETHICS

It is increasingly recognised that doctors cannot escape making a variety of ethical judgements in their practice. These vary from mundane practice decisions about accepting or rejecting difficult or unwelcome patients, perhaps unkempt, bedraggled and socially undesired by all, to issuing certificates against one's moral principles, to life and death issues. Students still receive insufficient formal education in ethical reasoning to help them prepare for such predicaments. It is just hoped and assumed that bedside teaching and scientific training will somehow equip them to make the right or the most professional decision without there being any clear idea of what 'right' or 'professional' means in this moral context.

Terminal care of the dying patient is an area that illustrates well mutually exclusive ethical courses of action. It is taught formally in the fourth year of the Queen's medical curriculum by close collaboration between the Departments of General Practice, Geriatric Medicine, Mental Health and Oncology, with various health and social work professionals, ministers of religion, and doctors and nurses from the Northern Ireland Hospice. Telling the truth gently is more morally complex than appears at first sight.

We try to make clear to students different and conflicting ethical positions, and discuss some mutually exclusive principles. These principles come into play in telling the truth to dying patients and may conflict if applied categorically. Two cases will illustrate the different moral dilemmas.

> A 26-year-old doctor, Campbell Moreland, became ill in 1980 and died of testicular cancer in 1982. His paper 'Whose choice? Whose consent?' was published by the Faculty of Medicine and used since for student reading.[13] It gives a poignant account of his illness, treatment and suffering. His experience shows that some doctors still practise in a pragmatic way without any sense of moral values. He used denial at the start of his illness despite a period of extensive investigations and at various stages in its course even after orchidectomy. At that stage he did *not* want to hear a specific diagnosis. He just drifted along in a state of depression hoping that it would soon be all over. Yet twelve months later when he was recovering from abdominal radiotherapy he bitterly resented being told a blatant lie by an unfortunate young doctor that his chest X-ray was perfectly normal, when he was riddled with lung secondaries and denial had been cast aside. He knew that he was terminally ill. He was physically frail, but intellectually active.

Truth-telling in my student days in a similar situation was a matter pf practical expediency to be avoided at all costs. Deception was the name of the game so as not to damage patient morale or shorten life or indeed offend the consultant in charge, whose policy of communication in these situations was usually not known. The young doctor lied in the wrong circumstances and rejected the

patient's autonomy and right to be informed of all the options and consequences. Campbell Moreland expresses this vividly: 'So often the doctor confuses his privileged position in the doctor-patient relationship with what he considers a right to choose for the patient'. He has no moral right to do so in many instances. He is simply caught between two conflicting options — that of preserving life and that of relieving suffering.

> Recently I was privileged to receive from a cleric a diary kept by a spouse in the practice, whose young husband had died. She had known for six months that the prognosis was hopeless but withheld discussion of the fact because her husband never seemed to consider that he was gravely ill and battled on bravely to meeting his daily commitments. He discovered the truth from his doctor only when close to death. He was quite shocked because he had always expected to recover. She wrote — 'He has been ill many times, had suffered bravely and without complaint, but he had always recovered'. She was torn with guilt and anguish that she had not told him sooner, but was afraid that by doing so she would have undermined his confidence or shortened his life. The patient had been well supported in his terminal illness by his wife, his family, the Church, a cancer specialist and the family doctor. When he was close to death, his wife asked him if he was very lonely thinking about death and he said he was. She wrote 'That night my husband had a struggle. He could not accept death and that the end was close. He said "We'll fight it. The doctors were not right before". I just held him closely to comfort him'. Unfortunately, the doctors were right this time and he died soon in a coma.

This case illustrates the anguish for the doctor of balancing deception and truth-telling in the interests of the dying patient, of infringing autonomy yet maintaining confidence and morale. Yet one must walk the tight-rope of honesty to achieve spiritual contentment and trust and confidence in the doctor-patient relationship to the very end.

The primary care setting provides a great array of problems which require ethical decision-making. Prominent among these are problems related to reproduction, including abortion, birth defects, infertility, contraception, sterilisation and sexual issues in general, and also pain control and patients' rights.

NATURE OF CONFIDENTIALITY

General practitioners are familiar with the problems confronting a family doctor who prescribed contraceptives to a 15½-year-old girl who is having illicit sex with a mature male. She is determined to continue the relationship, prefers the pill to alternative methods of birth control and refuses consent to her parents being informed. In 1980 the DHSS (London), in a Health Service Notice, issued guidelines for doctors in this type of case: 'A doctor was entitled in exceptional circumstances to prescribe contraceptives to a girl under 16 in England and Wales without the consent of parents'. Many people maintained that the circular encouraged or condoned unlawful intercourse. Mrs Victoria Gillick challenged the DHSS guidance in the courts on the grounds that the notice made doctors accessories to a crime and infringed the rights of parents over their children. In court the judge upheld the DHSS guidelines provided the doctor thought the girl competent and mature enough to understand all the issues involved. Mrs Gillick then contested this judgement in the Court of Appeal and in 1984 her appeal was allowed. The Court held that the ethical position in law was that parents are the

best arbiters of the child's interests and ignored patient autonomy. The see-saw legal battle continued and the Law Lords in 1985 upheld the DHSS appeal against the Gillick judgement and reversed the Court of Appeal's ruling.

The Law Lords defined the five exceptional circumstances under which a doctor could prescribe contraceptives to a girl under age as: (1) the girl understands; (2) she cannot be persuaded to tell her parents; (3) she is likely to begin or continue sexual intercourse with or without contraceptive treatment; (4) unless she receives treatment her health will suffer, and (5) her best interests require treatment without parental knowledge.

The ethical implications of all this for doctors are three-fold. The BMA maintains the principle of confidentiality to be paramount, but opponents claim that secrecy has no intrinsic moral value and would argue that it was more immoral to maintain the girl's confidence and deceive her parents. Gillick supporters argue that hormones are dangerous drugs and the supply of contraceptives infringes the principle of non-maleficence, is liable to harm the health of the patient, and encourages early promiscuity. Thirdly, under the Sexual Offences Act 1956 if a man has intercourse with a girl under 16 (England and Wales) he is criminally liable. Some may feel that a doctor would be acting immorally to collude in prescribing contraceptives, thereby transgressing the moral law of God and the law of society. Professor Kennedy[14] states that the doctor could be regarded in law as an accessory to crime only if he prescribed contraceptives in collusion with the male partner to encourage the under-age girl to have sexual intercourse.

In 1986 the last DHSS Guidelines were issued spelling out 'exceptionally, in cases where persuasion to tell the parents fails, the doctor should be free to prescribe without parental knowledge'. There the matter rests for the time being, but let me remind you of the BMA's five exceptions to the principle of *not* breaching confidentiality (BMA *Handbook of medical ethics*):[4] (1) when the patient gives consent; (2) when it is undesirable on medical grounds to seek a patient's consent, but it is in the patient's own interest that confidentiality should be broken; (3) when the doctor's duty to society overrides the principle; (4) when required for the purposes of medical research; (5) when required by due legal process. Secrecy is ultimately destructive of honesty and trust. Yet if the GP had informed the girl's parents without her consent, there would have been a family crisis. It is sometimes well-nigh impossible to choose a course of action which meets the teenager's health needs and at the same time does not violate the doctor's honest relationship with her parents. Underlying the Gillick arguments is the question of who should decide for the young. Lord Scarman revealed that the decision to override parental rights and responsibilities was not entirely a question of a doctor's discretion. He warned that a doctor must exercise his judgement properly, otherwise there could be possible criminal consequences, if he went outside the exceptional circumstances already defined by the Law Lords. Parents should normally decide, but how can they exercise this responsibility if they are in a state of ignorance of their child's sexual behaviour. In these circumstances it is difficult to avoid the conclusion that a doctor who knows the parents is the person to exercise this responsibility, because he is the one to whom the girl has gone for medical advice.

THE SELECTIVE TREATMENT OF BIRTH DEFECTS

Early in my career in the Jubilee Neonatal Unit I was confronted with the ethical problems posed by the treatment of severely malformed infants with spina bifida

and hydrocephalus. Many can be saved now from death by surgical treatment. Modern surgical advances and medical technology have brought great benefits but have blurred concepts of life and death and created huge ethical dilemmas for doctors. Lorber, a Sheffield paediatrician, assessed the results of early surgical treatment of spina bifida in babies ten years ago and identified the sharp ethical problems in management.[15] He chose babies with 'initial adverse criteria' after careful research and follow-up and put them into the 'non-treatment category'. This meant selecting some babies early on for nursing and medical care only — in other words, they would be kept clean and comfortable, and fed only on demand, but no measures would be taken to prolong their lives, such as restoration of fluid balance. He was supported in this ethical policy by the recommendations of a Working Party under the auspices of the Newcastle Regional Hospital Board, which laid down clear guidelines for doctors to follow in the selective treatment of spina bifida in infants.[16] Many would still argue that this policy is not moral. Lorber, however, makes it clear that he is against infanticide or active euthanasia, which he regards as both brutalising and illegal. He argues that less than half of all babies born in Britain with spina bifida survive to three years of age. In fact the less severely affected survive and most of the others die, often after many operations and much discomfort. Thus his severely affected babies, selected for non-treatment, would even if operated on have a very high mortality.[17] Medical dominance in decision-making is being challenged by society, but many paediatricians plead for doctors to be allowed to retain primary decisional power even if the chosen course of action involves the death of the infant.[18]

Lorber's selective treatment includes an assessment of the severity of the abnormality, of the likely effects of this upon the future quality of life of the infant after surgery, and of the likely burdens upon family and society. He argues further in justification of his utilitarian moral stance that survival of severely affected babies may disrupt family life, cause mental breakdown, suicide and even family break-up in some instances. Ranged against him, however, are the moral arguments of many philosophers and theologians. Harris, a philosopher, sees selective treatment as morally indefensible and in his view no different from active euthanasia.[19] The right to life of severely handicapped newborn infants should be accepted without question. Gillon believes, however, 'that it is because the newly-born infant is not a person, that it is justifiable in cases of severe handicap to allow it to die'.[20] Thus we see the conflict of moral views even amongst those concerned about ethical matters. In law the distinction that exists in medical practice between active and passive euthanasia is also recognised. The doctor who brings about the death of his patient by some positive slip is guilty of murder. In the case of the severely malformed infant, the doctor who withholds treatment is criminally liable only if there was a duty to provide treatment. If the child was likely to die in natural circumstances the law would regard treatment as merely postponing death. Cases on the quality of life have not to my knowledge come before the courts, and in the absence of legislation doctors and patients are still left to make these difficult ethical decisions about life and death in the treatment of severely handicapped infants.[21]

INFERTILITY AND FERTILISATION

There are serious moral problems raised by the 'reproduction revolution' brought about by the use of in-vitro fertilisation techniques. Soon in Belfast 'GIFT' techniques will be in use to overcome unexplained infertility in women with patent fallopian tubes. Gamete Intra Fallopian Transfer, which introduces sperms

and ova into the tubes, poses fewer moral problems than in-vitro fertilisation or implantation of a fertilised embryo into the uterus. In respect of the latter, for the moral purposes of this lecture I will stick to the Warnock Report recommendations.[22]

The birth of Louise Brown at Oldham in 1978 following IVF techniques to overcome the mother's infertility heralded a new era in the treatment of the disorder, which causes great psychological dysfunction, but rarely suicide. The success rate of IVF remains disappointingly low.[23] Replacing three or four embryos in the uterus offers the best chance of success, about a 25 per cent chance of pregnancy and a 14 per cent acceptable multiple pregnancy rate. It is also regrettable that only one of the 25 British IVF centres is operated under the NHS, the rest being privately managed. Experimentation over the past 10 years has brought into existence many left-over embryos, called 'spare embryos'. Speaking euphemistically they have died by the process of being washed down the sink. The temptation to do some form of research on these has proved irresistible to the scientists. The genetic material of the nucleus can be replicated into an infinite number of clones. Professor Ian Donald of Glasgow thinks such breeding to specification 'is indeed a threat to human life': what he calls 'a sort of scientific cannibalism'.[24] The only possible moral justification has to be expressed in utilitarian terms — the greatest good for the greatest number from the research. Yet it is virtually impossible to separate in moral terms issues of experimentation from therapeutic techniques of IVF because they are inter-dependent. Critics of the Warnock recommendations in this respect point to the lack of Christian judgement and the lack of emphasis on moral and spiritual aspects of the situation.[24, 25] There is some truth in this criticism because secular society was considered and a majority of members favoured a utilitarian position. They were undoubtedly deeply influenced by the potential benefits to mankind from research on human embryos. These range from enhanced knowledge of the process of conception, and of male infertility, to the genetic diagnosis of the embryos, to providing spare parts for a recipient of organ transplants in order to minimise the chances of tissue rejection. They seemingly elevated the advances of infertility treatment above concern for the welfare of human embryos. A compromise was adopted that embryo experimentation should be accepted up to 14 days after fertilisation only under licence, and unauthorised use would constitute a criminal offence. The cut-off point at 14 days is arbitrary in moral terms because, as Cameron says, 'if sentience, the ability to feel pain, is ultimately to be the criterion it is something which is readily capable of subjection to anaesthesia'.[25] This view, stressing the point in embryonic brain development, when the embryo becomes a 'human person', is rejected in moral terms by Christian theologians, although it must be taken seriously.

Society must lay down some new ground rules to deal with the new technology and its consequences for mankind. Gillon poses the moral question 'What do we mean by the term human being?'[26] This is relevant to all the major moral issues of life today including abortion and switching off life-support machines. This raises further questions: 'When does life begin?' and 'Is the embryo a person?'. Orthodox Christian theology teaches that the zygote, the fusion of sperm and egg, is a human being equipped with a unique genetic package. Holbrook maintains that our respect for the human embryo must be absolute and must not be qualified by consideration of the benefits for research.[27] Cameron believes that 'our definition of what is distinctly human must be broad enough to encompass

the product of conception from its earliest days'.[25] Tomlin argues that human embryo experimentation is a blatant violation of the Kantian principle that 'one should never treat a human being as a means to an end, but always as an end in itself'.[28] My understanding of Roman Catholic theology from the evidence presented to the Inquiry was that people are special, because human beings possess a soul from the time of 'ensoulment' at conception. Unfortunately, there is still disagreement in Christian circles as to when precisely this occurs[29] and this was reflected in the oral evidence received. The problem in the Inquiry was that no moral consensus could be found, which reflects all the views of society itself. A narrow majority held that the fundamental moral questions (about life itself, already mentioned), were not susceptible of straightforward simple answers. Warnock says 'the answers to such questions are complex amalgams of factual and moral judgements'.[22]

Having tiptoed through the tulips of the Warnock minefield, where does this leave the busy doctor? First, it has to be understood that experimentation on human embryos is something which has already happened and has resulted in IVF techniques being used to produce hundreds of babies. A recent Edinburgh survey of attitudes of women of reproductive age to IVF procedures and embryo research showed that 94% thought that IVF treatment should be definitely allowed in Britain and much the same proportion wanted it available and free on the NHS.[30] This may mean that Britain is more a secular than a Christian society, but clearly each doctor must follow his conscience in the matter; regardless of personal morals he must seek to make specialised advice in this field available to any female patient seeking a remedy for childlessness when the new techniques are appropriate. This causes great moral embarrassment to some young doctors who argue that by doing so they are in fact colluding in murder — the same, of course, applies to therapeutic abortion. Personal moral values have to be weighed against values of human compassion and contractual responsibilities to one's patient.

TEACHING MEDICAL ETHICS

Gillon's intensive survey of the teaching of medical ethics in the USA revealed much more formal pre-clinical teaching than in Britain. Informal ethics teaching takes place as in the British Isles at the bedside in the clinical years. There is general agreement that theory and practice should be integrated as early as possible.[31] My own survey of medical ethics teaching in the UK showed that medical deans could not quantify or comment on the quality of the teaching. A successful prototype course was first run by Len Doyal, a lecturer in philsophy, at University College, London, in 1985/86. It was the first of its kind developed in response to the 1980 GMC recommendations with regard to medical ethics teaching.[32] The format of each session is a short lecture or film followed by a large group discussion with 45 students. The course has been revised in 1986/87 to contain the following topics: moral reasoning and medical ethics; the rights and duties of doctors; morality and scarce health service resources; morality and paediatrics; the ethics of medical experimentation; a return to personal autonomy and individual rights; the ethics of prevention versus care; medicine, morality and under-development; medical ethics and education. Some of these issues are covered in our embryo 4th year ethics teaching sessions at Queen's and we use clinical situations to explore many more moral issues.

Baroness Mary Warnock believes that teaching of moral reasoning should take place in schools before entry to universities. This is not universal here and is

unlikely to become so. By the time students reach medical school, their moral character has been formed. We can, however, provide them with ethical knowledge and interpersonal skills to enhance their ethical behaviour. Furthermore, we must bring home to them the practical importance of ethical issues for the whole of society. We should encourage them to come to their own conclusions and help them to resolve conflict. Simple health economics must be taught, especially about the just distribution of scarce health service resources.

The time has come to make recommendations about the teaching of the topic in the future. My thoughts are best summarised in two recommendations of a Working Party of the Institute of Medical Ethics,[1] a group convened by the General Medical Council and the Nuffield Foundation.

1. Medical ethics teaching should recur at regular intervals throughout medical training, and time should be set aside within existing teaching for ethical reflection relevant to each stage of the student's experience.
2. Clinical teaching of medical ethics should normally begin from clinical examples. Such teaching should be exploratory and analytical rather than hortatory. Adequate provision should be made for small group discussions. Discussions should be supported by critical reading of relevant papers on medical ethics.

No one could gainsay either of these recommendations. They are met, albeit to a limited extent, in present formal teaching of medical ethics in the 4th year Joint Course in the Queen's medical curriculum. We seem to have got the format right and we have interested teachers. From time to time it may prove necessary to involve moral philosophers and representatives of the legal profession, much as we have done with spiritual advisers in care of the dying.

In conclusion, I have made explicit the relevance of medical ethics to clinical practice and offered a practical method of applying general ethical principles and moral doctrines to solve medical moral dilemmas. Your reaction and response will settle whether or not I was wise to choose such an abstract yet important topic in the wake of the I.M.E. Report. I found it a daunting task, conscious that doctors do not like theoretical lectures on moral philosophy. I will blame the choice on the vagaries of a professor of general practice, a peculiar hybrid by any standards. Universities and general practice are very different in structure and function. The former are intellectual and increasingly research-orientated, the latter is more intuitive and pragmatic. If I have managed to overcome to some degree the difficulties of my academic post it is in no small measure due to the enormous support of my colleagues in hospital and general practice, and the staff in the Department itself. Medical ethics is a vital aspect of medical practice. To summarise the theme of this address I quote Longfellow, 'Morality without religion is an empty shell, a kind of dead reckoning, an endeavour to find our place on a cloudy sea'.

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Review

Energy sources for intravenous nutrition

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SUMMARY

Controversy exists concerning the appropriate use of carbohydrate solutions and fat emulsions as energy sources in intravenous nutritional regimens. Current evidence suggests that glucose is the carbohydrate energy source of choice and that when infused with appropriate quantities of protein it provides cheap and effective nutritional support in the majority of patients and clinical circumstances. During glucose infusion, blood glucose and acid-base balance should be closely monitored and, when indicated, exogenous insulin should be added to the regimen to combat hyperglycaemia and improve protein anabolism. Fat emulsions, although expensive, may justifiably be used in patients with moderate or severe stress to provide up to 50% of non-protein energy, especially in circumstances where attempts to satisfy energy requirements exclusively with glucose would impose an additional metabolic stress.

INTRODUCTION

Intravenous nutrition is regarded as one of the most significant advances in medical and surgical management during the past 20 years. Several studies have documented a high incidence of clinical and sub-clinical malnutrition in hospitalised patients,[1,2] which is associated with increased morbidity and mortality. These complications of medical and surgical disease may be reduced by the appropriate provision of nutritional support by oral, enteral, or parenteral route. The therapeutic nutritional regimen should provide adequate protein and energy substrates to replete and maintain adequate nutrition and to match the increased metabolic demands of illness and infection.[3] The formulation of an intravenous regimen is based on the use of solutions containing essential and non-essential crystalline amino acids to provide protein requirements, the use of carbohydrate solutions or fat emulsions or a combination of both to provide energy, and the addition of minerals, vitamins, and trace elements to satisfy daily requirements. Although a standardised regimen containing about equal proportions of crystalline amino acids and dextrose with appropriate additives will satisfy the nutritional requirements of many patients, adjustments may be needed to meet the increased demand for all nutrients during infection, or to cope with special problems such as renal failure, hepatic dysfunction, protein intolerance and the paediatric patient.[3] Controversy exists concerning both the composition of amino acid solutions, and the most appropriate energy source for optimal utilisation in various diseases. This review discusses the use of hypertonic glucose solutions, glucose substitutes, and fat emulsions as energy sources in intravenous

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regimens for the management of hospitalised patients. These regimens are used in a spectrum of clinical conditions and the metabolism of these nutritional supplements under normal conditions, in starvation, and in various degrees of stress will be discussed.

ENERGY REQUIREMENTS

The relative energy requirements in health and disease differ. The basal energy expenditure of a normal 70kg man at rest is about 2,000 Kcal per day. Decreased food intake is accompanied by weight loss and a decrease in basal energy expenditure. Following elective surgical procedures, in the absence of significant complications, the post-operative energy expenditure will not ordinarily differ by more than 10% from pre-operative values. Previously well-nourished patients with multiple fractures may have an increase in basal energy expenditure of 10 – 25%, and in major infection, such as intra-abdominal abscess or peritonitis, there may be an increase of up to 50 – 75% above predicted normal levels. Sustained higher levels of basal energy expenditure (125%) may occur with major thermal burns.

The metabolic response to injury is classically described as being separated into two distinct phases – an acute phase in which there is mobilisation of endogenous substrates to provide energy, and an adaptive phase in which metabolism is dependent on the availability of nutrient substrates. These phases correspond to the 'ebb' and 'flow' phases of the metabolic response to trauma originally described by Cuthbertson in 1942.[4] The metabolic response to starvation differs from that of injury and infection, and it is important to realise that, in individual patients, varying degrees of starvation, injury, and infection may contribute to the overall changes in hormonal and substrate homoeostasis.

METABOLIC RESPONSE TO STARVATION

The sequence of events leading to death in starvation is usually decreased food intake, protein wasting, weakness of respiratory muscles, atelectasis, pneumonia, and death. The metabolic response to starvation has an initial and a late phase: the initial phase is directed toward maintaining glucose production to meet the needs of the brain, nervous tissue, and red blood cells (gluconeogenic phase), and the late phase toward minimising the rate of protein breakdown (protein-conservation phase). Fat derived from adipose tissue stores is the main endogenous fuel in all but the postprandial state and satisfies 85% of daily energy needs in prolonged fasting. During starvation, in the absence of an exogenous carbohydrate supply, there is an increase in glucose production and a reduction in extracerebral glucose utilisation. Blood glucose concentration declines and results in decreased circulating insulin and glucagon which stimulates lipolysis (providing non-esterified fatty acids for energy requirements of muscle and liver) and hepatic ketogenesis. Liver and muscle glycogen stores rapidly become depleted, and glucose production subsequently depends on gluconeogenesis from lactate and amino acids, principally alanine and glutamine from muscle protein. During the initial 72 hours of starvation, alanine output increases and hepatic glucose output is able to keep pace with the rapid rates of glucose utilisation in the brain. Pyruvate, lactate, and the glycerol skeleton of triglyceride are also used as gluconeogenic substrates. If fasting extends beyond one week, nitrogen loss progressively declines and there is a reduction of hepatic gluconeogenesis. Blood glucose levels remain unchanged and there is a reduction

in glucose utilisation. These changes are accompanied by an increase in circulating ketone bodies, which are formed from fatty acids in the liver. There is a reduced need for gluconeogenesis which is reflected in a decreased output of alanine from muscle.

METABOLIC RESPONSE TO INJURY AND INFECTION

Following the stress of injury or infection, the pattern of endogenous fuel substrate utilisation differs from that observed in uncomplicated starvation. The most obvious differences are protein wastage, hyperglycaemia, and anaerobic glycolysis with lactate production. Injury induces a wide range of integrated changes in haemodynamics, neuroendocrine secretions (in particular, insulin, glucagon, corticosteroids, and catecholamines), and tissue metabolism. Provided that the injury is not fatal, the immediate phase of depressed local metabolism is followed by a period of increased general metabolism due to the increased cellular activity of the repair process, elimination of damaged and devitalised tissue, and increased catabolism of protein. There is also increased oxygen consumption and heat production, and the increased nitrogen excretion closely parallels the increased energy expenditure.

The changes in energy metabolism are most important for survival and repair. There is increased sympathetic activity for 48 – 72 hours which ensures an adequate mobilisation of carbohydrate and fat stores, resulting in hyperglycaemia and increased plasma non-esterified fatty acids, but the rates of oxidation of both substrates are unaltered. Following the acute reaction to injury, which may last up to 72 hours, there is an increase in heat production and rise in body temperature associated with an increase in urinary excretion of nitrogen, inorganic sulphate, phosphate, potassium, and creatinine. The excess nitrogen is derived from catabolism of muscle protein and the oxidation of non-nitrogenous residues accounts for some of the extra heat production. This obligatory protein loss cannot be completely abolished in the immediate post-traumatic period, even with large intake of protein and calories. Protein catabolism is accelerated to a greater extent than protein anabolism and the prolonged proteolysis of muscle protein leads to excessive hepatic gluconeogenesis, depletion of muscle protein, weakness, reduction of protein synthesis, diminished enzyme function, and loss of immunocompetence.

Hyperglycaemia and a diabetic glucose-tolerance curve are characteristic of the response to injury and infection, despite a normal insulin response to hyperglycaemia. Glucose uptake by the tissues is unaltered, suggesting insulin resistance in the tissues. Adipose tissue still responds to hyperinsulinaemia by suppression of lipolysis. Alanine, lactate, and glycerol all provide an increasing flow of gluconeogenic substrate to the liver which releases more glucose under the influence of alanine-induced hyperglucagonaemia. There may be impairment of uptake of other metabolic fuels (non-esterified fatty acids, ketone bodies) leading to the oxidation of branched-chain amino acids derived from muscle protein to satisfy the local energy requirements of muscle. Thus, hyperglycaemia reflects an augmentation of the glucose pool to maintain glucose oxidation rates rather than a need for overall energy provision from proteolysis. Although the nitrogen excretion following injury parallels the increased resting metabolic expenditure and weight loss, the energy contribution of protein is only about 20% of daily expenditure, the residual energy requirement being met by mobilisation of fat stores.

ENERGY PROVISION

The substrate and hormone changes that characterise the responses to starvation, injury and infection are designed initially to ensure survival and subsequently to initiate repair processes at the expense of endogenous tissue stores, which further compromises host metabolism. It is against this complex biochemical background that nutritional support of the hospitalised patient is usually undertaken. Intravenous nutritional regimens are designed to replenish existing deficiencies, to minimise further tissue consumption, and to provide sufficient energy and protein substrates to stimulate and maintain anabolism and repair. An important limiting factor of intravenous nutrition is the ability of tissues to metabolise the infused nutrients: on the one hand, there is the requirement for large quantities of exogenous nutrient substrates to satisfy nutrient requirements while, on the other hand, local and general metabolic responses to starvation, injury and infection may reduce the efficient utilisation of those substrates. This may lead to unnecessary complications of therapy such as the over-enthusiastic infusion of hypertonic glucose solutions to the septic patient leading to worsening of pre-existing hyperglycaemia, excessive glycosuria, osmotic diuresis, increased fluid and electrolyte losses, dehydration, and non-ketotic coma. The most important determinant of outcome in a patient receiving nutrition exclusively by vein is the ability to supply and metabolise sufficient protein to compensate for the catabolism of endogenous protein, to synthesise acute phase proteins, to maintain immunocompetence, and to preserve the integrity of major organ systems. Protein economy and the utilisation of exogenous crystalline amino acids improves as non-protein energy provision increases and thus the success or failure of a nutritional regimen is dependent on the appropriate choice of a non-protein energy source.

There are essentially three practical methods of delivering non-protein energy in intravenous regimens — glucose, glucose substitutes, or lipids. Glucose is available in concentrations from 5% to 70% and may be used exclusively as the energy source provided minimal amounts of fat are given to avoid essential fatty acid deficiency. Glucose substitutes — fructose, sorbitol, xylitol — also are available in a range of concentrations, but they appear to have no particular advantage over glucose. Fat emulsions (10% or 20%) have a high energy value, but the daily dosage should not exceed 2.5g/kg body weight and should not make up more than 60% of the total energy intake. Each regimen has its advocates, but rational choice of an energy source has to take into consideration the type of patient, disease process, therapeutic goal, expense, substrate utilisation, method of delivery, and potential complications.

GLUCOSE

The average oral diet contains about 45% carbohydrate and 40% fat, and together these two energy-yielding substrates supply approximately 90% of daily energy requirements. Glucose infusions are used extensively in surgical practice, both to maintain hydration together with electrolyte solutions and as a source of energy. Glucose can be metabolised by all the tissues of the body and it is a prerequisite for protein anabolism. A normal person can assimilate up to 800g of glucose per day, but glucose is taken up by muscle and adipose tissue only in the presence of insulin. Many studies have documented improvement in cardiac, respiratory, and hepatic function as well as improvement in cellular function as a result of glucose infusion both with and without exogenous insulin. (Table I).

TABLE I

Relative merits of intravenous glucose

Advantages

- Readily available in a wide range of concentrations 5 – 70%
- Easily stored
- Cheap
- Stimulates endogenous insulin production
- Reduces proteolysis and gluconeogenesis

Disadvantages

- Hypertonic solutions require central infusion
- Glucose intolerance may require exogenous insulin
- Osmotic diuresis
- Lack of fat and essential fatty acids
- Hepatotoxicity
- Stimulates fat synthesis
- Increased CO_2 production
- Central venous thrombosis
- Septicaemia and bacterial infection
- Metabolic complications (acidosis, hypophosphataemia)

Glucose solutions are readily available in a wide range of concentrations from 5% to 70%. They are cheap and are easily stored. Five and 10% solutions may be infused via peripheral lines but higher concentrations require the use of a central vein with the inherent risks of mechanical complications and infection. Because of the range of concentrations available, each regimen may be tailored to the energy requirements of individual patients. Glucose infusion stimulates insulin production from the pancreas which enhances protein anabolism and reduces proteolysis and gluconeogenesis. In many patients, glucose may be used as the sole energy source.

The disadvantages of glucose as an intravenous energy source are usually related to two factors – firstly, the supply of glucose in excess of the energy requirements, and, secondly, changes in body metabolism as a result of injury and infection which interfere with the cellular metabolism of glucose. These conditions may produce hyperglycaemia and osmotic diuresis leading to fluid, electrolyte, and acid-base imbalance and requiring the use of exogenous insulin to maintain normoglycaemia. Excessive intravenous glucose may also lead to impairment of biochemical liver function tests, increased fat synthesis and deposition, hypophosphataemia, and increased CO_2 production. Due to the hypertonicity of the solutions, central venous thrombosis may occur and bacterial contamination with septicaemia is common unless a strict protocol is followed for the management of central venous lines. Infusion regimens that contain no fat will lead to essential fatty acid deficiency after several weeks. Concentrated glucose infusions should always be given with an adequate protein intake to avoid the development of 'iatrogenic kwashiorkor'.

The energy requirements in starvation and nutritional depletion without stress are relatively easily supplied by glucose infusion alone. However, there is an upper

limit to the rate of glucose oxidation, and endogenous fat continues to be used for a portion of the total energy requirements.[5] Excess glucose is converted to fat which is inefficient as lipogenesis consumes energy that is not recovered during subsequent lipolysis. In mild and moderate stress, there is usually hyperglycaemia due to increased gluconeogenesis rather than reduced glucose oxidation.[6] Glucose infusion will not completely abolish gluconeogenesis and fat oxidation and mobilisation of endogenous fat continues even when glucose is supplied in quantities that satisfy energy requirements. Large glucose loads may also decrease free fatty acid oxidation and cause additional stress by increasing oxygen consumption and carbon dioxide production and norepinephrine excretion in the urine.[7] Intolerance to glucose may be even more pronounced in the severely stressed critically ill patient and large quantities of exogenous insulin may be required.

Intravenous regimens containing crystalline amino acids and glucose as the non-protein energy source have been shown to improve nitrogen balance in a number of disease states and clinical situations.[8, 9, 10] The weight of evidence from clinical studies shows that, with adequate protein intake, nitrogen retention and utilisation improves as energy intake increases, until energy requirements are satisfied.[10, 11] Energy supply in excess of requirements produces no additional nitrogen sparing and may give rise to significant biochemical, hepatic, and respiratory complications.[8, 12, 13]

GLUCOSE SUBSTITUTES

Fructose, sorbitol, and xylitol have been suggested as alternative intravenous sources of carbohydrate when hyperglycaemia and significant losses of glucose in the urine are features of the metabolic response to injury and infection. This recommendation is based on their rapid metabolism compared with that of glucose, their 'insulin independence' and their similar protein and antiketogenic effects. However, studies of their comparative metabolism show that the term 'insulin independence' is misleading, as these substrates are rapidly converted to glucose in the liver, and further metabolism by extrahepatic tissues requires the presence of insulin.[14] The theoretical advantages of these solutions would therefore appear to be unfounded and are outweighed by their disadvantages. At high rates of infusion, significant metabolic acidosis, hypophosphataemia, and hyperuricaemia may occur, particularly in patients who are nutritionally depleted or who already have elevated plasma lactate levels as a result of their disease process.[15] If these solutions are used, they should be used cautiously and their infusion rates should not exceed 0.5 g/kg body weight/hour or they should be used in combination with glucose to minimise the risk of complications.[16, 17] However, the ease of monitoring blood glucose, glycosuria, and acid-base balance, and the use of appropriate exogenous insulin therapy when indicated suggests that glucose is the carbohydrate energy source of choice in intravenous regimens. The therapeutic success of glucose and insulin therapy in patients who are critically ill and severely stressed leaves few indications for the clinical use of glucose substitutes.[18]

FAT

Fat emulsions have been used extensively in intravenous regimens in Britain and Europe for many years, but it is only in recent years that extensive experience of the use of fat as an intravenous energy source has been obtained in the United

TABLE II

Relative merits of intravenous fats

Advantages
— Available in 10% or 20% emulsion
— Isotonic and may be infused peripherally
— Source of essential fatty acids
— High energy density
— No metabolic complications
Disadvantages
— Expensive
— Not recommended as sole energy source
— Not 'protein-sparing' when used alone
— Hyperlipaemia
— May inhibit white blood cell functions
— Hepatotoxicity
— Impaired pulmonary diffusion capacity
— Fungal infections
— Alterations in coagulation and thrombocytopenia

States. Emulsions of 10% or 20% soy-bean or cotton-seed oil are available, which are isotonic, have a high energy density, and may be infused via a peripheral vein. It is recommended that the infusion rate should not exceed 2.5 g/kg body weight/day and that fat should provide no more than 60% of the non-protein energy. Fat emulsions provide a source of essential fatty acids and deficiency can be prevented by supplying approximately 5% of energy requirements as polyunsaturated fat by the intravenous or enteric route. Apart from hyperlipaemia, there are few metabolic complications, although hepatotoxicity, inhibition of white cell function, coagulation defects, and thrombocytopenia may all occur. A further limiting factor is their expense in comparison with hypertonic glucose. (Table II).

When used alone, fat is not protein-sparing, the minimal improvement in nitrogen sparing being accounted for by the free glycerol present in the fat emulsion.[19, 20] In starved and nutritionally depleted patients, similar nitrogen balances have been observed in groups of patients receiving the same total energy and nitrogen intake when 83% of their non-protein energy was either lipid or hypertonic glucose.[21] In stressed hypermetabolic patients, there is a progressive decrease in nitrogen retention as the percentage of total energy provided by glucose decreases and by fat emulsion increases.[8] Other studies have shown similar nitrogen-sparing effects of the lipid and glucose systems in moderately injured, infected, and malnourished patients and it has been suggested that the choice between the regimens should be based on factors other than ability to improve nitrogen balance.[22] In the critically ill patient, at least two-thirds of the measured or predicted metabolic requirements should be supplied as glucose, and fat emulsions should be used as a source of essential fat and to stabilise body fat mass and increase body weight. In starvation, lipid clearance from the blood stream and its use as an energy source is very similar to the chylomicron and

appears to be enhanced by the simultaneous administration of glucose. In moderate stress, there is more complete oxidation of exogenous lipid and no additional stress associated with increased oxygen consumption, CO_2 production, and norepinephrine excretion or fatty liver seen in patients receiving glucose infusion for prolonged periods. In severe stress, the ability to clear fat emulsions is markedly impaired and fat oxidation is reduced.

ENERGY SOURCES — GLUCOSE VERSUS FAT

The non-protein energy requirements of an intravenous diet may be supplied by hypertonic glucose solutions or fat emulsions. In all situations, glucose is the carbohydrate energy source of choice as it is inexpensive, associated metabolic acidosis is unusual, and hyperglycaemia is easily treated with exogenous insulin.[15] In normal and starved patients, equal energy fat and carbohydrate regimens with amino acids produce similar nitrogen balances.[21, 23] In hypermetabolic patients with burns or infection, carbohydrate appears to have a greater impact on nitrogen retention than does fat. Nitrogen retention improves as carbohydrate intake increases, provided that total energy intake matches total metabolic expenditure.[8] The nitrogen-sparing effect of carbohydrate appears to be mediated through insulin, and additional nitrogen retention may be achieved with exogenous insulin.[24] The explanation of this apparent difference between fat and carbohydrate as energy sources in hypermetabolic patients is related to the muscle fuel deficit that exists secondary to a failure of keto-adaptive mechanisms and suppression of hepatic ketone body output by glucose. In addition, inflammatory tissues are glycolytic and have a major capacity for anaerobic metabolism. Endogenous fat is the primary fuel for skeletal muscle and hepatic gluconeogenesis, while glucose and lactate provide energy for the injured tissues.[25] Thus, fat emulsions will stabilise body fat and serve as an exogenous fuel, but will not affect nitrogen balance, whereas exogenous glucose stimulates insulin which reduces muscle proteolysis and nitrogen excretion.

Although fat emulsions appear to have limitations as energy sources in hypercatabolic, injured, or septic adults, it is important that some fat be given in depleted states to ensure that essential fatty acid deficiency does not occur. Skin rashes, thrombocytopenia, increased haemolysis, and impaired wound healing may appear after a period of several weeks of fat-free intravenous nutrition. The clinical abnormalities are accentuated by growth in children and the hypermetabolism of infection and are associated with low serum levels of essential polyunsaturated fats and a compensatory increase of saturated fatty acids. The ratio of the trienoic and tetraenoic fatty acids rises in deficiency states and may be used as a guide to the adequacy of replacement therapy with intravenous fat emulsions. Deficiency may be prevented by supplying approximately 4% of total energy requirements as polyunsaturated fat. In infected patients receiving intravenous nutrition with no oral intake, 500 ml of fat emulsion (Intralipid 10%) may be given on alternate days to satisfy this requirement and the triene/tetraene ratio is measured at intervals. Small amounts of polyunsaturated fat (safflower oil) may be given by tube if the enteric route is available.

Fat and carbohydrate may also have differing effects on body composition measurements. Although intravenous hyperalimentation is often associated with weight gain and positive nitrogen balance, it is only recently that direct measurement of changes in body composition has contributed to our knowledge of the tissue changes involved. A study of the relative merits of glucose and fat as

energy sources showed that in two groups of patients with gastrointestinal disease requiring intravenous nutrition, marked differences in body composition were noted after a two-week infusion period with the substrates.[17] The group receiving dextrose as its sole energy source gained weight due to gains in body fat and body water, but in the group which received 60% of its non-protein energy as fat, there was a significant gain of protein but not water and fat. The authors suggested that the differences in water retention might be particularly significant to the critically ill patient and indicated that more studies were necessary to define the respective roles of fat and carbohydrate as energy sources in several clinical situations. The ability to preserve muscle and visceral protein mass and stimulate anabolism is critical to the successful outcome of hypermetabolic illness, and it appears that this goal may be achieved with an adequate protein intake, and a modest energy excess utilising a range of nutrient mixtures.[27, 28]

The septic and injured patient seems to utilise endogenous fat preferentially as an energy source even when dextrose is administered in quantities above energy expenditure. Administration of a large dextrose load to hypermetabolic patients does not suppress net fat oxidation as it does in the depleted patient, but there is an increase in oxygen consumption, continued oxidation of fat, and an increase in the conversion of glucose to glycogen.[7] This is associated with an increase in CO_2 production which is not seen when fat emulsions are used. The excess CO_2 has to be excreted by the lungs, and in patients with infection and compromised pulmonary function, respiratory distress may be precipitated. In this situation, a large dextrose intake may represent an additional physiological stress. Fat emulsions must be used with caution in a patient with respiratory distress or 'shocked lung', as fat emboli may occur, further compromising respiratory performance.

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Pathways in the study of perinatal disease

The 3rd Royal Maternity Hospital Perinatal Lecture,
delivered on 10 October 1986.

J E Morison

For about fifty years I have actively studied the nature and cause of disease. I would like to explore a few aspects of our understanding over that period of disease as it affects the fetus *in utero* and the newborn baby. This is a period of life of special interest in that it often concerns the interplay of conditions which can arise in two separate individuals. It includes the study of developmental biology, the modifications imposed on the fetus by multiple disturbances in the maternal and fetal relationships and the many challenges the baby meets as it must rapidly adapt to an entirely new environment at birth.

To the clinician a disease may present as a complex of signs and symptoms. Often to the pathologist it is only the structural changes revealed by the naked eye or by the microscope. To appreciate in detail the structural framework of disease is of great value for its understanding. Often it imposes a useful discipline limiting useless speculation. Morphological descriptions alone tell us little of how diseases evolve, and, increasingly, for any real understanding we must think of both health and disease as a study in biology, and hope to understand them both by using and selecting relevant studies in all the life sciences. Pathology must be a dynamic study rather than descriptive and static, and must also relate to all studies on the living patient.

If for convenience we think of a disease as an entity, we can think of our understanding of it evolving and advancing along many different directions or pathways. Some of these may define its origin and behaviour more clearly and others may show its affinity with other biological events both normal and abnormal. Especially when pathways of investigation link up with others in allied disciplines, this may allow a rapid advance and widening of our understanding. Indeed, today almost all advances are made when pathways in apparently unrelated disciplines thus converge and unite. It must be accepted that many pathways that open with promise end in blind alleys, or at best make only a minimal contribution. However, today's cul-de-sac may be tomorrow's avenue of advance.

Before reviewing some examples of how researches have opened up pathways leading to a wider understanding, it is essential to know from where we started and where we are now. Access to the consensus of existing knowledge has advanced in the last three or four decades. Descriptions, for example, of congenital abnormalities, once only available by searching through dusty and poorly illustrated journals, are now well presented and often beautifully illustrated. We must rejoice that facts once in the possession of the few are now so generally available. With this information explosion a new problem arises. This is the

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multiplication of journals and monographs and their increasing cost, and the declining resources available to libraries for their purchase. The problem is not access to photostats of a few papers on a specific problem. It is the inability to read and to assess continually and critically all relevant studies and especially those necessary to prepare or revise a really comprehensive text, monograph or review. I believe this is now becoming nearly impossible with the resources available in many medical schools.

CONGENITAL ANOMALIES

Throughout history, man has been interested in congenital abnormalities and especially in the more bizarre malformations. Descriptions of the form and morphology of gross malformations have advanced relatively little in the last forty or fifty years. Sophisticated techniques have with increasing accuracy unravelled anomalies, such as cardiac malformations, during life rather than in the post-mortem room. X-rays are often essential even at post-mortem for precise diagnosis. Inborn errors of metabolism continue to operate throughout life and differ from the once and for all disruption of normal structural development responsible for a malformation. Some, such as cystic fibrosis, may show at post-mortem marked and progressive structural changes even in the perinatal period, others only such subtle structural changes as those of galactosaemia. Many inborn errors of metabolism can be identified only by chemical screening tests in selected population groups.

Important recent developments have been not in anatomical but in epidemiological studies. These have shown the widely different incidence of specific anomalies, but strangely not the total number of anomalies, in different racial groups. They have emphasised that affected individuals often show multiple and apparently independent anomalies. Recent studies of artificially aborted embryos have shown a higher incidence of abnormalities than at normal birth. It would seem that many early and spontaneously aborted embryos must be abnormal. Often the malformations, such as hare lip and polydactyly, recognisable in these artificially aborted early embryos, are no more severe than those in fetuses surviving to term. This would suggest that abnormalities often represent a more complex and lethal disorganisation of development than is structurally apparent. Related to this is the increasing recognition that aborted conceptuses often show a disorganised and sometimes bizarre arrangement of their chromosomes.

In the early part of the century, speculation as to the basis of abnormalities was along pathways now largely abandoned, and often seemed to point to familial inheritance. The simplest examples were recognised but the many different genetic and environmental influences contributing to and necessary for the expression of all but the simplest examples of genetic inheritance were not appreciated. Eugenists, overimpressed by selective breeding in animals, even raised false hopes of the elimination of many imperfectly defined defects.

Early in this century, experimental embryology was emphasising the effect of noxious chemical and physical influences on free-swimming embryos. In the forties, studies on mammalian reproduction and human pregnancies increasingly suggested at a low level of probability that environmental conditions might influence the incidence of malformations. These environmental influences became an acceptable basis for human malformations only with the recognition of the influence of rubella and of the embryopathic drug thalidomide. The emphasis on environmental influences was valuable, but numerous attempts to

identify other teratogenic agents, chemical or infective, operating alone in any significant number of anomalies have been unrewarding. Studies, such as those showing the effect of nutritional deficiences on the proper closure of the neural canal may suggest that, at most, environmental influences modify the expression of other, presumably multifactorial genetic factors.

A specified defect can only occur if a teratogenic agent operates at a relevant period of development, and for most defects this is long before the sixth to eighth week of menstrual age. If drugs are to do harm they must have been taken early, and, for severe defects, before many women are sure they are pregnant. The evidence does not support the present widespread concern, nor the judgements of American courts of law, that almost all drugs are potential teratogenic agents.

After the recognition of the basis of Down's syndrome in 1959, many useful paths to understanding abnormalities have come from the study of chromosomes, of groups of genes and even of individual genes. Abnormal chromosomal patterns and enzyme defects in cells taken from the early embryo may increasingly allow parents the choice of eliminating affected products. Attempts at genetic engineering will occasion even greater practical and ethical problems. There is also the increasing problem so common in medicine today of limited resources but ever increasing demand. It is undesirable to seek publicity and research funds by raising expectations of any early, general or widespread application of methods of genetic control which cannot hope to be fulfilled.

BIRTH TRAUMA

Physical birth trauma is now rare and, indeed, it was always rare in Belfast obstetrical practice. Statistics have always been unreliable. For long it was incorrectly thought by many that subarachnoid and intraventricular haemorrhage was traumatic. It is the result of anoxia operating in the actively developing sub-ependymal area of the immature brain. Again, pathologists, poorly trained in the technique of the perinatal post-mortem, can all too readily tear engorged intracranial sinuses and bridging veins and be deceived by blood escaping at the post-mortem. Small amounts of blood in the anterior and middle fossae may not be the cause of death. One may find blood pigment in relation to dural surfaces or in the tentorium long after birth and unrelated to illness or death. Haemorrhages into the scalp and even into skeletal muscles are rarely important. Gross injuries, such as subcapsular tears of the liver with resultant intra-peritoneal haemorrhage are exceptional. However, for a short period in the mid-sixties, extensive traumatic pulmonary interstitial emphysema with unrecognised pneumothorax was encountered here in a cluster of infant deaths. It was apparently due to imperfect control of apparatus used for artificial respiration. To hold the benefits of advances along any pathway demands perpetual vigilance.

PERINATAL INFECTIONS

Infections acquired in intra-uterine life and from the new environment during and after birth make a fascinating study. Some infections reach the fetus across the chorionic villi from the maternal blood, others spread from the amniotic sac before, or more often after, its rupture, and yet others are acquired in the birth canal or from the external environment.

We can chart hard-won knowledge of these infections in different ways. We can emphasise that some — rubella, toxoplasmosis, inclusion body disease and

syphilis — may infect from early in pregnancy and from the maternal blood. They may be manifest in a premature or term stillbirth, at the birth of a live-born infant, in the early days of life, in infancy, in childhood or even only in adult life. A great load of infection occurs around the time of delivery, and nearly all of this is bacterial and runs its course in the first three days of extra-uterine life. In others a wider spectrum of lesions is involved. Often the lesions are not specific for the disease, and for the recognition of many of these infections in their less overt form, and, to determine the agent responsible for many, we have to use new pathways made available by advances in microbiology. A few virus infections of interest, but mostly uncommon, occur just before, during or after delivery, and usually, but not always, from the mother. Considerable uncertainty exists for some, and there are difficult problems as to the route and time of infection and other problems such as those relating to vertical transmission of hepatitis B virus through many generations in some ethnic groups.

If the wall of chorion and amnion are examined after birth, a reaction by polymorphs may be found spreading in and around the blood vessels of the chorion and even into the wall of the umbilical vessels. It becomes increasingly frequent as labour is prolonged after the membranes rupture. About 10 per cent of placentas show the reaction. Bacterial cultures from the amniotic surfaces are of limited value and many normal placentas are contaminated. Many with reaction yield no organisms on conventional bacteriological study. For long, many maintained that this amnio-chorionitis was not an infection. Only a small proportion of the infants thus involved develop an inflammatory reaction in the lung in their first three days of life. However, a pneumonic reaction has been recorded in up to 15 per cent of all intra-partum stillbirths. Again organisms may or may not be recovered from the lungs.

Increasingly over the years, and with more adequate bacteriological techniques, organisms, including *Mycoplasma* and anaerobic and micro-aerobic bacteria, have been implicated in the reaction in the chorion and amnion and shown to invade the lungs and the blood streams. It has become increasingly certain that this inflammatory reaction is always infective. Occasionally the fetal membranes and even the lungs may be similarly infected by organisms entering across intact but devitalised membranes. Again, organisms, including sometimes virulent Group B streptococci, may be aspirated from the birth canal and cause pneumonia and fulminant septicaemia without this amnio-chorionitis. It should be emphasised that the reaction, involving as it does the large and relatively few vessels of the chorion, gives little opportunity for blood stream dissemination of organisms of low virulence or for absorption of toxins. It is different when the air spaces of the lungs, filled with amniotic fluid and with their numerous thin-walled capillary plexuses, are involved. There the organisms may proliferate as in a culture medium, cause an inflammatory reaction and allow toxic absorption and often a blood stream invasion. Of itself, amnio-chorionitis is probably rarely significant.

An association between perinatologists, pathologists, bacteriologists, virologists and immunologists has in recent years opened up many important pathways in the understanding of perinatal infections. Studies of immune tolerance to rubella in early embryos and of congenital immune defects in early life have contributed in turn to advances in immunology.

OXYGEN DEFICIENCY AND PERINATAL DEATH

All recognisable disease conditions — congenital, traumatic, infective and such miscellaneous conditions as blood and metabolic disorders — can explain only a proportion of perinatal deaths. About 40 per cent of deaths, and predominantly the deaths of premature infants, remain unexplained. These babies show changes sometimes minimal and difficult to evaluate. These are regarded as secondary to anoxia, or more correctly hypoxia. This anoxia might damage the parenchymatous cells of the brain or perhaps the heart and other organs, or could involve the interstitial tissues. Cellular damage may cause death in those who fail to establish respiration. In those who breathe for a period, the cellular changes sometimes found, especially in the brain, do not involve respiratory centres or areas concerned immediately with survival.

Changes in blood vessels and support tissues are often prominent, and especially in premature infants. Thin-walled and poorly supported blood vessels rupture in the rapidly developing sub-ependymal matrix around the brain ventricles, and, less importantly, in the subserosal tissues over viscera, and sometimes into the lung substance. More important is the accumulation of oedema fluid interfering with oxygen transfer in the body and lungs, and in the septa of the lungs perhaps splinting the tissues and impeding respiratory movement. This fluid crosses the placenta readily from the relatively large maternal blood volume, and its escape into fetal tissues is therefore not opposed by fetal haemoconcentration. In anoxia of some duration this is serious and comparable to overhydration by an intravenous drip in later life. There must be concern about the influence of overhydration on absorption of amniotic fluid from the distal air spaces.

All babies, whatever their cause of death, may show in some degree these changes since tissue anoxia is a universal terminal event. Those dying during or after birth from anoxia arising from causes outside their own body, and which I have designated as extrinsic or environmental anoxia, can and should be so recognised only when a most meticulous study excludes all other known causes of death. When an infant dies from extrinsic, as opposed to intrinsic or secondary, anoxia we must expect to find the cause in unfortunate conditions in its environment operating before or during delivery. These are essentially the concern of the obstetric side of the perinatal team. They may be briefly reviewed.

Oxygen levels to the fetus may be impaired by a few maternal extra-placental influences, such as maternal circulatory collapse, haemorrhage or severe anaemia. These and prolapse of the cord and other obstetrical complications may erode or destroy the capacity of even a healthy placenta to sustain an adequate oxygen level to the fetus. Close co-operation and frank discussion between the obstetrician and the pathologist is always essential in perinatal studies and here clinical data are often more important than any anatomical findings.

In the search for other causes of extrinsic anoxia we are concerned with the utero-placental unit. As in every organ there is here a reserve of function. There are efficient and less efficient placentas. The reserve varies from patient to patient. As pregnancy advances it tends to decline relative to the increasing fetal demands. It may decline differently for different functions. Biochemical measures of various metabolic functions do not necessarily measure oxygen transfer. However, their decline and any failure of the fetus to grow must be in some degree disturbing. Some infants may start with better placentas than others and should survive more degenerative change. The recognition by histological study that a grossly normal

placenta had a lowered reserve at birth is more difficult than many will admit. Morphometric studies of the total area of the villi and of the capillary networks where transfer occurs are tedious and only a few are available. They have revealed something of the attrition of the smaller 'breathing' villi towards term and of its acceleration in toxaemia. Attempts to assess that this has occurred in a normal or toxaemic pregnancy by transmitted light or phase contrast microscopy and by detecting an increase in the stroma of the villi, thickening of the basement membranes, or an increase deposit of fibrinoid material in and on the smaller villi are all without any quantitative basis and are all subjective. Dramatic gross lesions, such as a retro-placental haemorrhage abrupting the villous placenta, are rare but probably not all are recognised. Multiple infarcts may be impressive, but often more significant are diffuse degenerative changes which may or may not co-exist. Admittedly a large red infarct occurring very shortly before birth may sometimes escape recognition.

It now seems increasingly probable that the various conditions, known and unknown, producing a low reserve placenta operate through changes in the decidual vesels and those of the uterine wall and with resultant disturbances of the intervillous circulation. The inescapable difficulty is that these vessels are left in the uterine wall as the placenta tears away through the maternal decidua and are not available for study. Changes may be seen in the shed placenta, but it is still uncertain what changes are most significant as an index of functional impairment. It is against this background that we must welcome progress in monitoring at intervals during late pregnancy the pattern of fetal blood flow through the umbilical cord.

FACTORS IN THE INFANT MODIFYING INTRINSIC ANOXIA

We have still many unanswered questions as to how anoxia or an anoxic episode, however induced, threatens the life of the newborn. Does it operate alone or are other factors sometimes or often concerned? Indeed, we may be overlooking something else of importance. Some anoxic lesions, such as sub-ependymal haemorrhages, are lethal. Oedema of tissues and especially of the lungs progressively impairs oxygen transfer. In the forties we were too content simply to echo Drinker's dictum 'Anoxia begats anoxia', but in essence it is true. Hydrogen ion and electrolyte disturbances occur and progress if uncorrected, but are now usually controlled.

In any failure to achieve and maintain extra-uterine respiration, lung function is concerned, and some deficiency must occur here especially in those children in whom respiration is readily established but becomes progressively less satisfactory. There is a wide variation in the intra-uterine age of the premature infants thus affected, but lung development may not always reflect fetal age. It did seem from a study of the Harvard material by the limited histological techniques available in 1946 – 47 that neither fetal age, birth weight nor infant length consistently measured structural maturity. However, any structural differences in lung development on any definition of maturity seemed entirely insufficient to be related to the outcome. Later, neoprene injection studies and micro-dissection of the more terminal air spaces showed better detail in three-dimensional studies and especially the scarcity of the elastin support structures in the lungs of premature infants. Some knowledge of lung structure was gained, and it is still just possible that the elastin support of terminal air spaces develops in response to intra-uterine breathing movements and at any given fetal age may show

meaningful individual variations. However, no anatomical basis, apart from that of gross immaturity, was found sufficient to explain why some infants die from respiratory distress. This was not to open a pathway for significant advance. Personal research moved into other areas, and in perinatal pathology to the study of the placenta.

About this time interest generally moved to Gruenwald's work on surface tension at the aqueous-air interface in the air spaces and its control by a surfactant substance so that air spaces would neither over-expand on inspiration nor collapse fully during expiration. Surfactant production is dependent on the maturity of lung cells secreting it. Measured by assay in the liquor amnii, is is only in part related to fetal age. It is not useful to return to old fatalistic concepts that some infants die simply because they are premature even in the sense that their enzyme mechanisms for synthesis of surfactant are relatively immature. Other factors, including anoxia, may contribute to surfactant deficiency at birth and in the first few days. With increasingly successful therapy the deficiency is now often transient and there is rapid maturation of synthesis after birth. Problems still remain of the significance of an episode of anoxia and of surfactant and perhaps other factors in any failure to adapt to extra-uterine respiration.

Often on critical analysis we cannot properly ascribe a perinatal death to one single cause. Anoxic conditions leading to oedematous lungs and tissues predispose to infection, and bacterial infections spreading in these oedematous tissues may produce deceptively little reaction. The venous congestion of anoxia may enhance any bleeding from torn venous sinuses in the skull. Again too often we are all inclined to accept death as due to some congenital anomaly of very doubtful relevance.

Progress has been made and the pattern of advancing, ramifying and sometimes divergent paths has changed and is almost unrecognisable from that forty years ago. Endless highways and byways beckon and must be explored. I wish all of you success and adventure and as much pleasure and excitement as we have had over the last half-century.

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Shadows

Annual Oration at the opening of the 1986 – 1987 teaching session, Royal Victoria Hospital.

F S Grebbell

It is almost 160 years since Dr James McDonnell delivered an address to the students entering the Belfast General Hospital. Since that time it has fallen upon a member of this staff to welcome those students who have commenced their first year in the clinical branches of medicine. This year it is my privilege and honour to address and welcome you on behalf of the medical and dental staff of this hospital, a hospital with a great tradition and one which, I believe, is the 'leaven that has leavened the whole lump'. As your hospital work of the next three years unfolds before you, and you are instructed in the many branches of medicine, in the various clinics, lecture rooms, and at the bedside, I hope that you will come to appreciate the immense practical value of a thorough understanding of radiological principles; that you will get to know their worth, limitations, dangers and to some degree the cost of such a service along with its financial implications, especially as diagnostic radiology now plays such an important part in the making of clinical decisions and in patient management.[1]

In the United States of America it is not uncommon for medical students to receive many hours of formal radiological teaching. The student may also elect to attach himself to the radiology department for a period of one month. For this to obtain in the United Kingdom, additional university academic departments of diagnostic radiology would heve to be created — something which the Education Board of the Royal College of Radiologists has been pressing for, for many years. The creation of such departments would, however, depend upon the willingness of the State to finance them. There has been a technological revolution in radiology in the last three decades which has made it a most exciting and engaging discipline. Some would say that a high degree of intelligence and the ability to use effectively advanced technology is an important asset in medicine as practised today. Such technology, however, should not be permitted to distance you from the patient, who above all else requires compassion, tenderness and understanding. Samuel Johnson said: 'To live without feeling or exciting sympathy, to be fortunate without adding to the felicity of others or afflicted without tasting the balm of pity, is a state more gloomy than solitude — it is not retreat but exclusion from mankind. Marriage has many pains, but celibacy has no pleasures'.

I propose to talk about the early days of radiology, present day imaging, its cost and its future. This is not intended to be a comprehensive record of the discipline, and I have purposely refrained from commenting on the life of Roentgen or the history of radiology in the Royal Victoria Hospital as both subjects were admirably described by the late Dr David Porter in his Oration on 'The new photography' in 1962.[2] An eminent American paediatric radiologist, John Caffey, who died in

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1978, wrote: 'Shadows are but dark holes in radiant streams, twisted rifts beyond the substance, meaningless in themselves. He who would comprehend Röntgen's pallid shades, needs always to know well the solid matrix whence they spring. The physician needs to know intimately each living patient through whom the racing black light darts, and flashing the hidden depths reveals them in a glowing mirage of thin images, each cast delicately in its own halo, but all veiled and blended endlessly. Man — warm, lively, fleshy man — and his story are both root and key to his shadows; shadows cold, silent and empty'.[3]

Sir James Young Simpson, a Scottish obstetrician, who in 1847 discovered the anaesthetic properties of chloroform, prophesied that 'by electrical and other lights we may render the body sufficiently diaphanous for the inspection of the practised eye of the physician or surgeon'. On Friday 8 November 1895 Professor Konrad Roentgen discovered X-rays. It was a chance discovery, as so often occurs in science. Such were Fleming's discovery of penicillin, Jenner's of vaccination and Becquerel's discovery of the radioactivity of uranium salts. It is somewhat ironic that an English scientist, Sir William Crookes, had, some 16 years prior to Roentgen's discovery, unknowingly produced X-rays but had failed to recognise the fact. As Pasteur counselled 'chance visits only the mind that is prepared'. As with all new discoveries, there were those who belittled and scorned the 'new photography' as it was then called. When the future King Edward VII was shown the X-ray of a hand (which incidentally required a 20-minute exposure) he was reputed to have exclaimed 'how disgusting'. Going the rounds of the music halls was the well-known ditty deriding the discovery,[4] which went as follows:-

'The Roentgen rays, the Roentgen rays,
What is this craze?
The town's ablaze
With the new phase
Of X-ray's ways.

I'm full of daze,
Shock and amaze,
For nowadays
I hear they'll gaze
Thro' cloak and gown,
And even stays,
Those naughty, naughty Roentgen rays'.

Fortunately eminent medical men such as Sir Robert Jones and Sir James MacKenzie Davidson realised the decisive part that the 'new rays' could play in the practice of medicine and surgery. They immediately set about establishing the new science as an important addition to medical practice. At this time the early pioneers were unaware of the more sinister aspects of the effects of the 'new rays' on the body tissues. Unfortunately many of the early workers suffered epilation and skin damage with some suffering severe disfiguration to their hands and fingers. Later the vulnerability of the haemopoietic system to radiation was recognised and in 1921 Hermann Müller was awarded a Nobel Prize for demonstrating that X-rays could cause mutations.

Prior to the discovery of X-rays, knowledge of the disease was limited to the clinical examination, supplemented by post-mortem findings should the patient die. The new science of radiology was to change all of this. As early as 1897 contrast media was introduced into radiology when Cannon at Harvard fed

bismuth to cats (and by 1899 to human beings) in order to demonstrate the gastro-intestinal tract.[5] The first cystograms and micturition studies of the bladder were carried out in 1905 and 1907 using colloidal silver which in 1918 was replaced by the safer and cheaper sodium iodide.[6] During the 1914–18 war, research in radiology practically ceased as the discipline was directed towards the diagnosis of fractures, foreign bodies and gas gangrene. In 1918 Dandy performed the first ventriculogram when he introduced air through a trephine hole in the skull using a thin needle.[7] In 1922 Sicard and Forestier introduced lipiodol into the subarachnoid space as an aid in the localisation of spinal cord tumours.[8]

Egaz Moniz[9] was born in 1874 in the village of Avanca in northern Portugal. He became an eminent neurologist and was also involved in politics. In 1926 when a dictatorial government came to power in Portugal, he deserted politics and devoted his time to neurological research. It was this research work which eventually led, in 1927, to the injection of 25% sodium iodide into the carotid artery of a patient and to the demonstration of intracerebral tumours. This pioneer work by Moniz led to the establishment of a Portuguese school of angiography which became famous throughout the world. From the age of 23, Moniz had suffered from gout, which severely affected his hands, and all his angiographic techniques were performed by his junior colleagues. In 1949 he was awarded the Nobel Prize in physiology and medicine, not for his superb work in angiography, but for the more uncertain technique of frontal leucotomy.

Arthur Schüller[10] was also born in 1874, in the city of Brunn in the province of Moravia which, at that time, was part of the Austro-Hungarian Empire. He was appointed to the chair of neurology and psychiatry at the University of Vienna in 1910 where he attracted students of radiology from all over the world. He became known as the father of neuroradiology and was the first to recognise and interpret correctly the calcified pineal gland in 1906. His name is also associated with Hand-Schüller-Christian disease. His first book, in 1905, *An atlas on the radiography of the skull,* was a classic of its time, as was his comprehensive monograph in 1912 on *X-ray diagnosis of the head.* With the rise to power of the Nazis in Germany, he fled to Australia where he continued to practise medicine, although his two sons, who had remained behind in Europe, were exterminated in a Nazi concentration camp.

Following the discovery of X-rays, radiology was adjudged to be a diagnostic discipline. It has, however, played an important part in excluding disease and thus in alleviating mental stress. It has successfully monitored the efficacy of medical and surgical treatment. The demonstration of normal body structures and their variations of normal have added considerably to the knowledge of the anatomist and has led to a greater understanding and recognition of the diseased process. In 1940 Bentley and Leitner, working in the field of preventive medicine, introduced the first 'mass mini-service' into Great Britain for the detection of pulmonary tuberculosis.[11] This was a sequel of Manuel de Abreu's work in 1936/7 when he carried out a large-scale survey on tuberculosis in Brazil which led to the 'mass method' being employed worldwide. At this time physicians were reluctant to admit to medical students that in the absence of signs and symptoms active tuberculosis could be demonstrated by chest X-rays. Yet as far back as 1917 Osler had said 'In skilful hands the study of such cases with the Roentgen rays is of great value'. The mass mini-service also proved to be of signal benefit to the coal mining industry in the diagnosis of pneumoconiosis. An interesting

anecdote on the subject of preventive medicine involved Queen Amelie, the wife of the unfortunate King Carlos of Portugal who was assassinated. She decreed that her ladies-in-waiting should have their chests X-rayed in order to demonstrate the misshapenness of their thoracic cages due to tight lacing.

In the last three decades there have been major changes in radiological procedures. These are the imaging techniques of nuclear medicine, ultrasound, computed tomography, magnetic resonance imaging and digital subtraction angiography. The discovery of isotopes cannot be credited to any single individual. The scientific genealogy of isotope imaging can be traced back to Henri Becquerel, a Parisian who invented nuclear chemistry, for which he was awarded the Nobel Prize for physics in 1903, and Lord Rutherford, a New Zealand-born British physicist who in 1906 discovered the alpha, beta and gamma rays for which he received the Nobel Prize for chemistry in 1908. Radioactive isotopes were not produced artificially until 1934 when Curie and Joliot produced radioactive phosphorous by bombarding aluminium with alpha particles. It was not until the early 1960s that the clinical use of radioisotope scanning became routine in medicine, and it was only in 1966 that isotope scanning was introduced into the Royal Victoria Hospital. In 1971 the first gamma camera was purchased and in 1977 the radioisotope department obtained its first computer.

Ultrasound, as practised today, evolved from an idea by Paul Langevin, a French physicist, who, during the first world war, devised a means whereby submarines could be detected by the use of high frequency sound waves. This technique was called ASDIC, an abbreviation for Anti-Submarine Detection and Investigation Committee. In 1958 Professor Ian Donald, in Glasgow, applied this principle to demonstrate the fetus in utero, and this technique is now used extensively in obstetrics, paediatrics and in adult organ scanning. Its great benefit is that it is non-invasive and free from the biological hazards of ionising radiation. The first ultrasound scanner on this site was installed in the Royal Maternity Hospital in 1968.

Computed axial tomography, more commonly referred to as CT, was invented by Godfrey Newbold Hounsfield, a British scientist, in 1972. This new invention was, without doubt, the greatest advance in diagnostic radiology since Roentgen's discovery. It has revolutionised completely my own specialty, neuroradiology. Hounsfield's interest in physics and mathematics originated in his childhood. He was brought up on a Nottinghamshire farm, the youngest of five children. Here he became greatly intrigued with all the electrical and mechanical apparatus which one associates with farming — the generators, the binders and the threshing machines. He constructed electrical recording machines and even launched himself from the top of a haystack in a home-made glider whilst investigating the principle of flight. At the outbreak of the second world war he joined the Royal Air Force as a volunteer reservist, becoming eventually a radar mechanic instructor. While working for EMI in 1967 an idea occurred to him from which was to develop both the technique of computed tomography and the EMI scanner. For this outstanding work he became the recipient of many honours and decorations, culminating in the Nobel Prize for medicine and a knighthood. The Royal Victoria Hospital obtained its first CT scanner in 1977, and five years later this was replaced by a high resolution whole body scanner. It was a great tragedy that Britain failed to capitalise on this brilliant scientific invention. In 1980 EMI pulled out of the scanner market after suffering huge losses in the face of overseas

competition from Europe, the USA and Japan, whose scientists exploited Hounsfield's invention leaving Britain well behind in the field of CT technology.

The principle of magnetic resonance imaging (MRI) is not new. It has been used in biochemical laboratories to monitor metabolic reactions in the human. Felix Bloch of Stanford University and Edward Purcell of Harvard University, more than three decades ago, were responsible for the basic research which laid the foundations for the later development of the present imagers. They were awarded the Nobel Prize for physics in 1952. The great benefit of MRI is that it can generate images of the body structures without using ionising radiations. Computed tomography provides information which is basically anatomical; MRI would appear to be capable of more discrete discrimination between normal and pathological tissue and also of supplying information regarding the functional state of internal organs. As a standard of comparison of proven clinical value computed tomography will not easily be equalled but there is no doubt that MRI, which is now in its sixth year of clinical use, has passed the stage of being a scientific tool. It has become a most important diagnostic mode which will increase significantly the contribution of radiology to clinical medicine and teaching. It is my opinion that to remain in the forefront of modern medicine such a modality must be easily accessible and furthermore sited where it most benefits the population as a whole. In the USA, of every dollar spent on new imaging modalities in 1986, it is estimated that 23 cents will have gone towards MRI but only 14 cents towards CT.[12]

CT and MRI have not always been confined to hospital practice. Radiology was first used to investigate mummified material in 1896. Professor Ian Isherwood of Manchester used CT to investigate two mummies — a female named Khary and a male, Asru — and added considerably to the knowledge of Egyptology by producing transaxial body sections. In 1984 a naked body, apparently male, was found in a Cheshire bog. CT and MRI investigations demonstrated that he had been garrotted, had had his throat cut and had a fractured skull. He had also probably been stabbed in the chest, and the remains of his last meal of unleavened bread was identified in his stomach. It was suggested that he had been the victim of a ritual killing, and this 2,500-year-old murder case (the Pete Marsh Murder, or Lindow Man) became of great interest to Scotland Yard forensic scientists because of the novel methods of investigation. In 1985 CT was also used to determine the age of some twelfth century timber beams excavated from an archaeological site at Billingsgate. Images of the rings inherent in all timber were matched against a reference template, enabling exact dating to be made. The reconstructed pier, five metres long by two metres high, in the Docklands museum, will be the largest preserved wooden artefact in the United Kingdom.

Digital subtraction angiography was first introduced into the Royal Victoria Hospital in 1982. It is a progressive development from intravenous aortography which was initiated in 1958 by Bernstein and his colleagues.[13] In selective cases it removes the necessity for the more hazardous procedures of conventional angiography. Many of the radiological procedures used today for diagnostic purposes are also used therapeutically. Using percutaneous catheterisation, arteries can be occluded or dilated and the blood flow reduced to, or therapeutic drugs introduced into, tumours. Biliary stones can be removed percutaneously and kidney stones can be crushed with sound waves from a lithotripter machine. Needle biopsies can be performed through tiny percutaneous punctures using image intensification computed tomography or ultrasound.

The financing of the radiological department is one of the most expensive items in the hospital budget. It is now recognised that the rate of growth in the 'hi-tech' specialities, of which radiology is one, has been faster than the service can afford. The annual X-ray budget in the Royal Group of Hospitals at the present time is running at approximately £3,000,000 per annum. A large field gamma camera can cost over £200,000. The total replacement of a remote control screening room can cost up to £400,000, a lithotripter machine approximately £1,000,000. The capital cost of the present CT scanner was approximately £650,000 and, allowing for capital depreciation over seven years, it requires an annual budget in the order of £300,000. A magnetic resonance imaging machine will cost from £750,000 up to £2,000,000 depending on the degree of sophistication. The choice, therefore, for example between buying X-ray equipment, helping to build a geriatric unit or maintaining adequate staffing levels becomes one of subjective judgement.

Since the inception of the National Health Service in 1948 numerous re-organisations have taken place. The first was in 1974 when the hospital and community services were integrated. Re-structuring took place in 1982, and in 1984, following the Griffiths Report, when General Managers, patterned on industrial models, were introduced. This latter change certainly did not increase the influence of the medical and nursing staffs, although the same cannot be said of the administrative staff. In fact has this change improved the quality of care to the patient, or has it all been a huge conjuring trick of which Merlin would have been justly proud? As far back as 1976, Mr Paine, the then Governor of the Bethlem and Maudsley Hospitals, said that 'management must be the servant of the service and not its master and that the prime function of the administrator is to enable the clinicians to achieve their full potential in caring for the sick'.[14] He also pointed out 'that patients come to Health Services to be treated and not administered'. These re-organisations were presumably initiated to increase the efficiency of the Health Service. Efficiency usually means doing the same for less cost, now called efficiency savings. It is, however, quite incredible that within 10 years of the re-organisation of the National Health Service in 1974 the administrative and clerical staff had increased by approximately 77,000. In these times of cut-backs, some disguised as genuine cost improvements, which are affecting doctors, nurses and other therapists, perhaps a closer look should be taken at the administrative and clerical side where many, although not all, remote from patient care, are involved in work created by a clumsy and expensive management structure. You may recall the Grand Inquisitor's song from *The Gondoliers* where:-

> 'Lord Chancellors were cheap as sprats
> And Bishops in their shovel hats
> Were plentiful as tabby cats
> In point of fact, too many'.

I mentioned earlier that one might have to choose between several alternatives such as buying X-ray equipment and helping to build a geriatric unit. Perhaps the choice would be made much easier if the millions spent on the ever escalating administrative structure were available for all. Failing this, a remark made by Professor Howard Jacobs of the Middlesex Hospital comes to mind — 'the most economical way to save money is not to treat patients'. This point was further developed by Mr Timothy Mathews, the administrator of the same hospital, who said 'we will save £500,000 by shutting down 250 beds. The medical staff want us to carry on but we have to watch the budget. If we don't shut down, the DHSS

will take the running of the hospital out of our hands. So it is better to ration the number of patients'. Further on the question of cost efficiency savings, the radiologist can play an important part by advising clinicians about the value of available options in order to help achieve a diagnosis, thus avoiding expensive, unnecessary and superfluous investigations and at the same time saving the patient much inconvenience. This can best be achieved by a combined approach, and is basically an exercise in communication which will become more important as new diagnostic modalities appear with advancing technology. It has also now been proved that capital expenditure on new techniques is cost-saving and not inflationary.

What of the future? Looking back over 35 years I have witnessed a steady advance in radiological technology. On looking forward I see no end to the process. As students, your careers lie in the future. I would, therefore, like to speculate with you about the future of radiology, especially if you agree with Bertrand Russell that to care intensely about what will happen after one is dead is the mark of a civilised man. In attempting to predict the future I am reminded of those ironic words of Alvin Toffler, purported to be a Chinese proverb: 'To prophesy is extremely difficult — especially with respect to the future'. The technological revolution will see digital images stored on some form of computer medium which could be readily viewed on a TV terminal, rather than X-rays on the traditional light box. Silver, a rare and expensive element, will thus be replaced by the much cheaper silicon. Envelopes and piles of film, much to the delight of radiologists and secretarial staff, will become things of the past. Clinicians in outpatient departments, wards, operating theatres and seminar rooms will have their own terminals which will relay up-to-date and past radiological investigations. No longer will be heard the familiar and frustrating cry 'Where are the previous films?' If current technological trends continue, smaller and smaller structures will be identified with increasing clarity. Resolving powers in images of living matter may tend towards or even equal those normally preserved for pathological specimens. Apart from this increase in spatial resolution we are likely to resolve tissues of similar composition. Already white and grey matter in the brain can be distinguished in certain imaging modalities. In addition to these spatial and contrast resolution advances we will see body functions taking place in increasing detail. Nuclear medicine and positron emission tomography in particular show great promise in this context. Could it be that some day it might be possible to observe thoughts!

Advances in three-dimensional imaging such as computer graphics, stereo projections and holography could lead to images becoming more tangible, thus relating more closely to objects which we view in our everyday experience. Magnetic resonance spectroscopy, which could well become one of the most important diagnostic modalities in medicine, may lead to non-invasive biopsies and tissue characterisation. Spectroscopy can also generate information about tissue metabolism, such as the oxygen supply to tissues, and may become valuable in cerebrovascular and coronary artery disease.[15] Tissue characterisation may also become a reality using diagnostic ultrasound as the mini-computer is replaced by the micro-computer. It may even become possible, using ultrasound, to obtain images through the intact skull. A word of caution — when contemplating new technology and therapeutic measures it is worth remembering the words of Alexander Pope:

'Be not the first by whom the new are tried
Nor yet the last to lay the old aside'.

Will modern technology surpass the diagnostic accuracy of the clinician? It was Lord Kelvin, the Belfast-born scientist and mathematician, who said: 'When you can measure what you are speaking about and express it in numbers you know something about it, but when you cannot express it in numbers your knowledge is of a meagre and unsatisfactory kind'. The question has, I believe, been answered by the distinguished immunologist Sir Macfarlane Burnet, who summarised the situation thus: 'I can see no escape from the contention that, if judgement is to be based on experience, then a machine, which can give accurate weight to all the relevant information and express the judgement in terms of a quantitative probability, will give a more acceptable answer than any clinician. It will still be for the physician to interpret the pattern, but this time he will know that all the measurable data have been given due weight'.

This morning I hope that I have conveyed to you the essence of the progress which has occurred and may occur in diagnostic radiology. I trust you will realise that it is no longer sufficient for you to understand the past. It is even insufficient to limit your understanding to the present, a present which is vanishing rapidly in a world of accelerating technology. I hope, therefore, that you will learn to concentrate some of your thoughts on long-term expectations about the future. Before concluding I would like to pay tribute to the nursing and paramedical staffs of this Hospital who have borne the brunt of staff cut-backs over the last few years. Through all their frustrations they have continued to show great fortitude, dedication and loyalty to this Hospital and above all to the patient. It was of such as they that Thomas Gray wrote:-

'Along the cool sequester'd vale of life
They kept the noiseless tenor of their way'.

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Spinal anaesthesia for surgical correction of fracture of the proximal femur

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SUMMARY

One hundred and one patients underwent surgical correction of fractures of the proximal femur under spinal anaesthesia. There were 14 deaths in the first three months following surgery. Advancing age, poor pre-anaesthetic status, reduced pre-operative mobility and deteriorating mental function were reliable prognostic indicators of fatal outcome. Spinal anaesthesia for this type of surgery may well be the technique of choice because it avoids the use of drugs which depress the respiratory, cardiac and central nervous system. It also reduces the need for potent post-operative analgesics with similar depressant effects, and may afford some protection against thromboembolic complications. The very low early mortality in this series testifies to the safety of the anaesthetic technique.

INTRODUCTION

Fractured neck of femur in the elderly is a common condition associated with substantial morbidity and mortality.[1] These patients occupy surgical beds for long periods of time at a considerable cost to the National Health Service in terms of manpower and services. The main principles of management include early operative fixation, early post-operative mobilisation and early recognition and treatment of post-operative complications. There is evidence to suggest that these management aims may best be achieved by early surgery under spinal anaesthesia.[2] It is established policy in this unit to employ such a technique and the objective of the present study is to identify those peri-operative factors which predispose to a fatal outcome.

PATIENTS AND METHODS

Patients over 60 years of age requiring surgical repair of femoral neck fractures were studied. In line with current policy, these patients were placed on the next available operating list following essential pre-operative preparations. No patient was refused surgery on anaesthetic grounds. All patients were subsequently followed up for three months post-operatively.

The following information was obtained for each patient: Mental state on admission — lucid at all times or confused (assessment was purely subjective and

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was made by the house officer and anaesthetist); pre-admission mobility — fully mobile or restricted; general health status (graded 1 – 5) in accordance with the American Society of Anesthesiologists (ASA) classification,[3] (See Table I); fracture type – subcapital, basal/transcervical, intertrochanteric, subtrochanteric; cardiac status — ischaemic heart disease, hypertension, dysrhythmia, congestive cardiac failure; respiratory status — chronic obstructive airways disease, lower respiratory tract infection; blood urea and haemoglobin concentration.

Only essential pre-operative interventions were performed. These included correction of hypovolaemia by blood transfusion and the treatment of dehydration, congestive heart failure and identified sepsis. Prophylactic antibiotics, either ampicillin and flucloxacillin or erythromycin were given pre-operatively and continued for 10 days after surgery. It was not Unit policy to employ drug prophylaxis against deep venous thrombosis.

Spinal anaesthesia was induced in the lateral position using bupivicaine 0.5% or 0.75% in a dose of 2 – 4 ml according to patient size. Pre-loading of the cardio-vascular system with intravenous fluids was not performed because of the poor cardiorespiratory status of these patients. Hypotension due to spinal anaesthesis was corrected with a methoxamine infusion (0.004%) as required.

Surgery consisted of fixation with either Smith-Petersen trifin pin and plate, Jewett blade plate, or Austin Moore hemiarthroplasty replacement. Surgery was performed by the same team consisting of consultant orthopaedic surgeon and/or registrar. No attempt was made to mobilise patients until the tenth post-operative day. Any significant post-operative complication was noted, and the times from operation to 'fit for discharge' and to 'actual discharge'. Results were analysed using the Chi squared test, Fisher's exact probability test and the Student T test.

RESULTS

A total of 106 unselected consecutive patients were studied. Five of these patients were excluded because satisfactory spinal anaesthesia could not be established. Fourteen of the 101 patients died within three months following operation. There were no deaths within the first 24 post-operative hours. One patient died during the first post-operative week, and a further six by the end of one month.

The mean age was 77 years, the majority (78%) were female. There were no deaths in the 19 patients under 70 years of age. In the 45 patients between 70 and 79 there were three deaths. There was no significant difference in mortality between males and females. There were 11 deaths in the over-79 age group, which was statistically significant ($p < 0.01$) compared with the other age groups. Mortality in groups 1 and 2 (2%) of the American Society of Anesthesiologists classification was significantly lower ($p < 0.01$) than groups 3 and 4 (26%) (Table I).

Admission mental state and pre-admission mobility (Table II) were further prognostic indicators of outcome. There was a mortality of 34% in confused patients compared with 6% in lucid patients. The mortality among those with restricted mobility was 25% compared with 2% among the fully mobile. Both these differences are statistically significant ($p < 0.01$).

There was a substantial incidence of pre-operative medical problems, particularly cardiovascular, in the patient population (Table III). The only condition amidst

TABLE I

Mortality related to the pre-operative classification of the American Society of Anesthesiologists

Pre-operative grade	*Number of patients*	*Deaths*	*Percentage*
1	1	0	0
2	50	1	2
3	44	9	20
4	6	4	67

Grade	*Physical status*
1	Healthy.
2	Mild systemic disease.
3	Severe systemic disease, limiting activities.
4	Incapacitating systemic disease which is a constant threat to life.
5	Moribund patient not expected to survive 24 hours with or without surgery.

TABLE II

Effect of mental state and mobility on outcome

	Number of patients	*Deaths*	*Percentage*
Mental state:			
lucid	72	4	6
confused	29	10	34
Mobility:			
full	49	1	2
restricted	52	13	25

TABLE III

Medical problems on admission in 101 patients with fractured neck of femur

Condition	*Number of patients*
Ischaemic heart disease (ECG diagnosis)	92
Ischaemic heart disease (with symptoms)	37
Hypertension (on treatment)	27
Congestive cardiac failure	11
Permanent dysrhythmia	17
Chronic obstructive airways disease (on treatment)	26
Lower respiratory tract infection	7
Elevated blood urea (sustained) >10 mmol/l	10
Anaemia requiring blood transfusion	8
Diabetes mellitus (on treatment)	8
Cerebrovascular accident	5
Other	18
Concurrent drug therapy	65

this widespread spectrum of disease found to contribute significantly to mortality was a sustained elevation of blood urea greater than 10mmol/l after adequate hydration — the associated mortality was 40% ($p < 0.01$).

There was no correlation between the type of fracture or method of fixation and survival, nor was there any significant relationship between survival and the delay between injury and operation. The mean duration of operation, including the establishment of anaesthesia, was 95 ± 4 minutes. Hypotension requiring methoxamine infusion occurred in 32% of patients. The duration of surgery and frequency of hypotension did not differ between survivors and non-survivors. Intra-operative complications included tachyarrhythmias in three patients and severe hypotension in one patient, the latter in association with the use of bone cement. This patient suffered a moderate hemiplegia which resolved only partially, but all four of these patients were alive at three months. Eighteen per cent of patients did not require post-operative pain relief, and the remaining patients did not require any analgesia for 8–16 hours post-operatively. Headache, probably of spinal origin, developed in one patient and responded to simple analgesics.

Serious complications developed in 31% of patients, of whom 14% subsequently died (Table IV). A single cause of death could not be identified in most instances since a number of pre-terminal conditions usually co-existed and post-mortem examination was not performed. Bronchopneumonia, congestive cardiac failure, myocardial infarction and cerebrovascular accident were all associated with a high mortality. There were no deaths recorded among the four patients with diagnosed thromboembolic disease. The only death in the first post-operative week (day two) was due to bronchopneumonia which had been present prior to surgery.

TABLE IV

Serious post-operative complications and mortality

Condition	*Number of patients*	*Percentage fatal*
Congestive cardiac failure	6	67
Myocardial infarction	5	60
Bronchopneumonia	22	59
Cerebrovascular accident	4	50
Fixation failure	5	20
Wound breakdown	10	20
Thromboembolism	4	0

The median delay between operation and mobilisation was 14 days. The median delay between operation and clinically 'fit for discharge' was 25 days (mean 31 days) and the median delay between operation and 'actual discharge' was 38 days (mean 53 days). This added delay was due to a variety of social reasons. The total bed days attributable to social reasons was 1081. At the conclusion of the three-month follow-up, 72% of the patients had been discharged and 14% remained hospitalised. Full pre-injury mobility was achieved by 23% of the discharged patients and the remainder were mobile with the support of an aid.

DISCUSSION

Fractured neck of femur in the elderly is a common condition with a high mortality. The largest published series of over 2600 patients by Gallannaugh and colleagues reported a mortality of 20% at one month.[1] The mean duration of hospital stay was 34 days. A major disadvantage of a large multicentre retrospective study is the absence of standardisation of anaesthetic and surgical management. Furthermore, most series have data with general and regional anaesthetic techniques combined, even though there is evidence to suggest that the latter have a lower morbidity and mortality.[2] The present review is confined to the standardised anaesthetic and surgical management employed in a single unit.

The low mortality in our series, 1% at one week and 14% at three months, compares favourably with other studies in which the mortality frequently exceeded 20% at three months.[4] It is now recognised that patients surviving the first three post-operative months have a similar life expectancy to the general population.[4] The single most important contributor to mortality in the present study is advancing age.[5] Men may have a significantly higher mortality than women,[6, 7] although we did not find this. The other well-recognised factor influencing outcome is the pre-operative classification used by the American Society of Anesthesiologists which is related closely to advancing age.[8]

Impairment of pre-admission mobility and of mental state on admission was associated with a mortality of 34% and 26% respectively. An elevated pre-operative blood urea of greater than 10 mmol/l, not attributable to dehydration, was also an indication of a fatal outcome. The delay between injury and operation, the duration of surgery, or the occurrence of intra-operative complications had no bearing on subsequent outcome. We were not able to demonstrate a significant association between fracture type and mortality, although several workers have found increased mortality in patients with trochanteric fractures.[9, 10]

A single cause of death was in most cases difficult to identify. Commonly, death was preceded by two or more conditions, such as bronchopneumonia, congestive cardiac failure, cerebrovascular accident and myocardial infarction. Notably absent from this list is pulmonary embolism which Davis and Lawrenson suggest is responsible for up to 30% of peri-operative deaths and is frequently misdiagnosed as bronchopneumonia.[11] We made no specific investigations to detect pulmonary embolism, and it is therefore possible that this was a cause of death in some patients. Some authors recommend spinal anaesthesia for surgical fixation because it induces vasodilatation of the leg vessels and increases peripheral blood flow while maintaining cardiac output. In the present study all four patients with diagnosed thromboembolic episodes survived.

Pre-operative morbidity added considerably to the surgical problems in this series. No single condition was statistically associated with a fatal outcome, but not surprisingly those patients with the largest number of complications were more likely to die.[12] These conditions also contributed to a median duration of hospital stay of 38 days (mean 53 days), which was further prolonged by delay attributable to social reasons.

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Radionuclide monitoring in Northern Ireland of the Chernobyl nuclear reactor accident

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SUMMARY

Northern Ireland received higher radiation doses due to the radionuclide contamination from the Chernobyl nuclear reactor accident than did the south of England. Levels of radioactive iodine (^{131}I) and caesium (^{137}Cs) in cows' milk in Northern Ireland increased to 166 and 120 Bq/l respectively in May 1986, but had decreased by factors of one million, and of twenty-five, respectively, by 1 September 1986. The resultant radiation doses represent less than one per cent of those received by a Northern Ireland individual over a period of 40 years from natural background radiation sources. The added risk to any individual from the Chernobyl accident will therefore be very small and may best be judged in the context of the enormously greater risk of death due to potentially preventable diseases, such as smoking-related lung cancer, and coronary heart disease.

INTRODUCTION

The Chernobyl reactor accident occurred in the Ukraine, USSR, on 26 April 1986 and the radionuclide cloud reached its peak over Northern Ireland on 3 May 1986, based on increased dose rates measured in Newtownards, Co. Down,[1,2] retrospective computer modelling,[3] and meteorological data.[4]

A considerable number of radionuclides have been detected in the Chernobyl emissions in the UK,[5] of which ^{131}I, ^{137}Cs and ^{134}Cs are major long-lived beta and gamma emitters of great importance in the human food chain. ^{131}I has a physical half-life (see glossary of terms) of eight days and is particularly important, as it is concentrated principally in the thyroid gland, with a biological half-life in the normal thyroid of about 120 days.[6] ^{137}Cs and ^{134}Cs, which have physical half-lives of 30 years and two years respectively, become uniformly distributed throughout the whole body and are slowly excreted from the body with a biological half-life of about 110 days.[6] These radionuclides can enter the human body from a number of sources including rainwater, milk, leafy vegetables and meat. Cows' milk is a particularly sensitive early indicator and a potential major contributor to human radiation dose.

The radiation dose from ingestion of a particular radionuclide is determined by the total radioactivity ingested and the fraction retained, the types and energies of radiations emitted by the radionuclide, the biological pathways for the

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radionuclide throughout the body, its concentration in particular organs and the length of time it remains in the body (the effective half-life). This investigation reports a number of radionuclide measurements made on rainwater, drinking water and cows' milk, from which estimates are made of typical radionuclide ingestions and resultant radiation doses. Consideration is then given to the possible effects of these radiation doses on the Northern Ireland population.

Thyroid uptake monitoring was also performed on four Northern Ireland students who returned from the USSR following the Chernobyl accident. One of these students was evacuated from Kiev, 100 km from Chernobyl, in the days following the accident. The other three Northern Ireland students were 650 – 900 km from the affected area and remained in the USSR for a further two months.

METHODS

Levels of ^{131}I and ^{137}Cs in rainwater, drinking water and pasteurised cows' milk from the Belfast, Lisburn and Rostrevor areas were measured at dates between 3 May and 5 June 1986. Further measurements for ^{137}Cs in cows' milk were made up to 1 September 1986. Limited facilities precluded measurements of ^{134}Cs and of radionuclide levels in other food products.

Samples were collected of rainwater draining from roofs in Belfast, Lisburn and Rostrevor. Mains drinking water samples were collected from the taps in the same houses. The water in the mains was supplied from reservoirs of the Department of the Environment, Water Division. Cows' milk samples were collected as delivered by the milkman in these areas.

Ten millilitres of each sample were placed in a sealed glass test tube and counted in a Tracerlab Gamma Set 500 counter with 3″ × 3″ NaI(Tl) crystal and 1″ × 2″ (deep) well. ^{131}I was measured using a 300 – 420 keV energy window to detect the 366 keV gamma ray photons of ^{131}I and a 647 – 677 keV window was used to detect the 660 keV gamma ray photons of ^{137}Cs. Each sample was counted for 4 – 14 hours to achieve acceptable statistical accuracy and these counts were then compared with background counts determined for the same time period for a distilled water sample, prepared before Chernobyl, which contained no radioactivity. The activities of ^{131}I and ^{137}Cs in each sample were determined by comparing the significant counts in the appropriate channel with the counts obtained from accurately known standards. A correction was made for Compton scatter of 660 keV photons of ^{137}Cs to the window used for ^{131}I. Allowances for radioactive decay from collection time to measurement time were made to give the radionuclide activity in each sample at collection time. The minimum detectable levels were 18 Bq/l for ^{131}I and 3 Bq/l for ^{137}Cs and experimental errors for the measurements were ± 23 Bq/l for ^{131}I and ± 8 Bq/l for ^{137}Cs at 99.7% confidence limits.

The effective half-lives of ^{131}I and ^{137}Cs in cows' milk were then determined by applying a computed least-squares exponential fitting procedure to the available experimental data from this investigation and that reported by the Northern Ireland Office for pasteurised milk for all the manufacturing plants in Northern Ireland between 5 and 19 May 1986.[1,2] These Department of Agriculture samples had been measured by British Nuclear Fuels plc using similar gamma ray spectrometry techniques.

Direct measurements of the amounts of ^{131}I in the thyroids of local members of the public were not made as these would have been close to the limits of

detection. The amounts of ^{131}I in the thyroids of typical Northern Ireland adults were estimated instead from the mean measured levels of ^{131}I in fresh milk on 5–19 May on the assumption that these levels continued to decrease with the mean computed effective half-life of ^{131}I in milk. It was assumed that milk was the chief source of ^{131}I and that 30% of ingested ^{131}I is deposited in the thyroid,[6] where it remains with an effective half-life of 7.6 days. Daily milk consumption per person for Northern Ireland is estimated to be 0.36 litres (0.63 pints).[7,8]

Thyroid activity monitoring for the four Northern Ireland students who returned from the USSR was performed using an Ekco 2" × 2" NaI(Tl) scintillation detector, a J & P high voltage supply, amplifier, pulse height analyser and scaler (Table I). Count measurements were made to detect 330–400keV and 605–700keV photons corresponding to ^{131}I and ^{137}Cs respectively. The NaI(Tl) crystal was kept flush with its collimator to increase detection efficiency of photons from the neck. Counting times of 15 minutes were used to achieve acceptable statistical accuracy. Background count measurements were made with the same energy windows to determine whether the counts detected were significant above background. Measurements were also made with accurately known standards in a perspex neck phantom in order to quantify the count-to-becquerel (see glossary) relationship for these radionuclides. Twenty-five millilitre samples of blood and urine obtained from the students were monitored for ^{131}I and ^{137}Cs, using the method described for radionuclide level assessment.

TABLE I

Details of four Northern Ireland students returned from the USSR

Student	A	B	C	D
Sex	M	F	F	F
Age	20	20	20	20
Residence in USSR	Kiev	Leningrad	Voronezh	Leningrad
Distance from Chernobyl (km)	100	900	650	900
Return date from USSR	1 May 1986	Late June 1986	Late June 1986	Late June 1986
Monitoring date at Royal Victoria Hospital	6 May 1986	30 June 1986	30 June 1986	8 July 1986

RESULTS

For rainwater, the maximum level of ^{131}I found was 94 becquerels per litre (Bq/l) in a sample collected in Lisburn on 3 May 1986. ^{137}Cs data is not available for this sample, which corresponded with the arrival of the Chernobyl cloud over Northern Ireland. ^{131}I levels in rainwater decreased below the levels of detectability (18Bq/l) within a few days. No drinking water sample was found to contain detectable levels of ^{131}I or ^{137}Cs at any time.

For cows' milk, the maximum level of ^{131}I found for this investigation (Regional Medical Physics Service data) was 91Bq/l for a sample from Belfast on 7 May 1986, which compares with a maximum value of 104Bq/l reported in the Greater Belfast area on 5 May 1986,[1,2] and the peak value for Northern Ireland of 166Bq/l (see Table II). The mean ^{131}I levels in cows' milk in three regions of Northern Ireland are shown in Fig 1 with data from this investigation for Belfast,

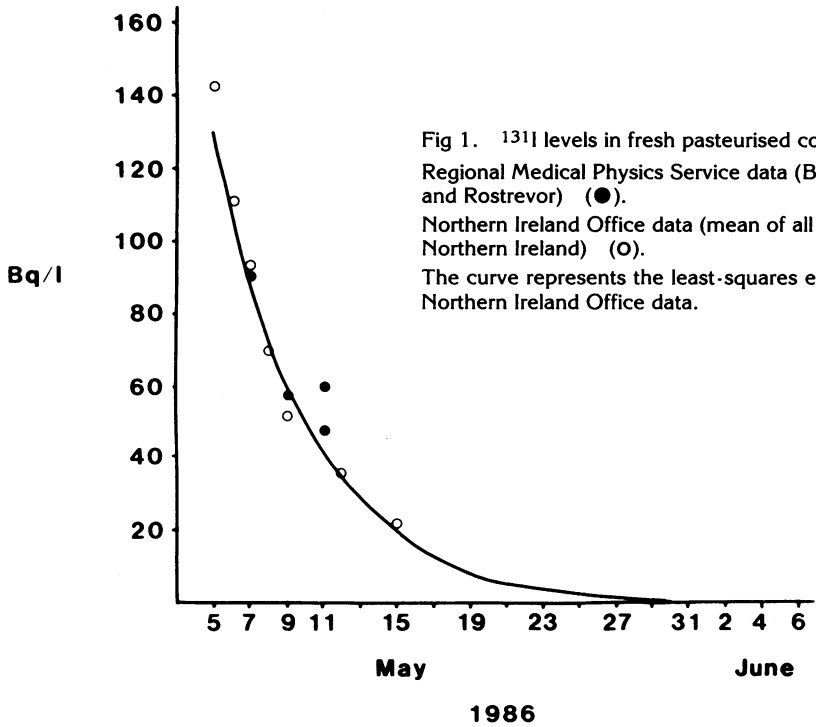

Fig 1. ^{131}I levels in fresh pasteurised cows' milk.
Regional Medical Physics Service data (Belfast, Lisburn and Rostrevor) (●).
Northern Ireland Office data (mean of all values for Northern Ireland) (o).
The curve represents the least-squares exponential fit to Northern Ireland Office data.

Lisburn and Rostrevor areas for comparison. The maximum level of ^{137}Cs for this investigation was 51Bq/l found for both Belfast and Rostrevor areas on 11 May, which compares with the maximum value of 78Bq/l reported for the Greater Belfast area on 8 May,[1,2] and the peak value for Northern Ireland of 120Bq/l (Table II).

TABLE II

Maximum levels (Bq/l) of ^{131}I and ^{137}Cs in cows' milk in Northern Ireland

Region	^{131}I		^{137}Cs	
	Maximum levels	Date	Maximum levels	Date
Belfast, Lisburn and Rostrevor*	91	7 May 1986	51	11 May 1986
Greater Belfast, South Antrim and North Down**	104	5 May 1986	78	8 May 1986
South Down and East Armagh**	156	5 May 1986	96	8 May 1986
Co. Fermanagh, Co. Tyrone, Co. Londonderry & N. Antrim**	166	5 May 1986	120	7 May 1986

*Regional Medical Physics Service data.
**Northern Ireland Office[1] data.

The ^{137}Cs levels in cows' milk in the Belfast, Lisburn and Rostrevor areas (Regional Medical Physics Service data), and those from Greater Belfast, South Antrim and North Down (Northern Ireland Office data) are shown in Fig 2. ^{137}Cs levels in milk delivered in the Belfast, Lisburn and Rostrevor areas had further

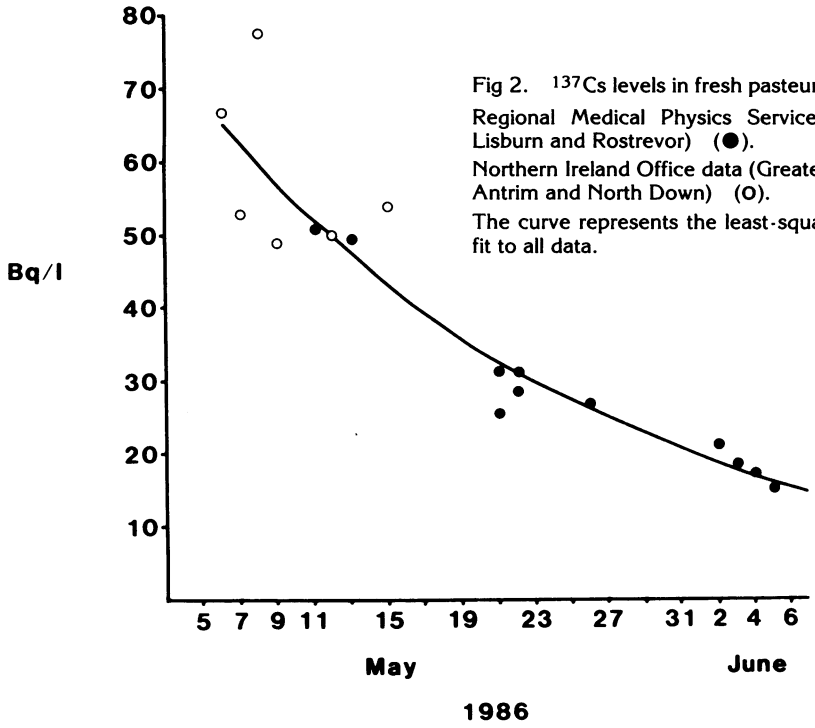

Fig 2. ^{137}Cs levels in fresh pasteurised cows' milk.
Regional Medical Physics Service data (Belfast, Lisburn and Rostrevor) (●).
Northern Ireland Office data (Greater Belfast, South Antrim and North Down) (o).
The curve represents the least-squares exponential fit to all data.

decreased to less than 3 Bq/l by 1 September 1986. The effective half-lives for ^{131}I levels in cows' milk were 2.3, 3.3 and 4.1 days for the three regions in Northern Ireland defined in Table II, and the mean effective half-life for ^{131}I was estimated at 3.3 days. The effective half-life for ^{137}Cs in cows' milk was 15 days.

The radionuclide monitoring data for the four Northern Ireland students who returned from the USSR are given in Table III.

TABLE III

Radionuclide monitoring data for four Northern Ireland students after return from USSR

Student	A	B	C	D
Thyroid activity (Bq)				
^{131}I	280 ± 50*	< 20	< 20	< 20
^{137}Cs	84 ± 47*	< 20	< 20	< 20
Blood activity (Bq/l)				
^{131}I	Not	< 18	< 18	< 18
^{137}Cs	monitored	< 3	< 3	< 3
Urine activity (Bq/l)				
^{131}I	< 18	< 18	< 18	< 18
^{137}Cs	< 3	< 3	< 3	< 3

*Statistical errors of ± 3 sd (99.7% confidence levels) are given. Thyroid activity estimate is subject to a further uncertainty of ± 50% due to possible geometry differences between thyroid depth in subject and ^{131}I standard depth in the neck phantom.

DISCUSSION

These measurements and those reported by the Northern Ireland Office[1,2] confirmed that ^{131}I and ^{137}Cs levels in milk were only a small fraction of the respective Derived Emergency Reference Levels of 2000 Bq/l and 3600 Bq/l,[9] at which consideration would be given to introducing counter-measures to reduce radiation doses to the public. The finding that radionuclide levels were below the levels of detection in drinking water is not surprising in view of the large dilution provided by the reservoir water supply system. A knowledge of the effective half-life of a radionuclide in a food source such as milk is one important factor in assessing the potential radiation dose to humans from food consumption. The effective half-lives found for ^{131}I and ^{137}Cs in cows' milk show reasonable agreement, considering experimental errors, with figures of 4.9 days[10] for ^{131}I and 10.5 days[11] for ^{137}Cs reported for Great Britain for the removal of ^{131}I and ^{137}Cs from grassland by both physical decay and natural removal processes following the Windscale nuclear reactor accident in October 1957.

The amount of ^{131}I accumulated in the thyroid of a typical Northern Ireland adult consuming an average of 0.36 litres of fresh pasteurised milk daily is estimated to have increased to 45 Bq in mid-May and then decreased to about 4 Bq by mid-June 1986. This estimated amount for Northern Ireland residents is considerably greater than the mean value of 18 Bq measured for the thyroids of eight adults from South London between 10 and 22 May.[12] These had been measured in a specially constructed room with low background radiation. The higher result for Northern Ireland is readily understandable since there was less rain in the south of England during the passage of the Chernobyl cloud, whereas Northern Ireland had sporadic heavy rain leading to greater radionuclide deposition on vegetation. Radionuclide levels in the south of England[5,12] have been lower than those reported for Northern Ireland in this investigation.

Using the Northern Ireland Office data from 5 to 15 May 1986, and assuming an intake of 0.36 litres of cows' milk daily with effective half-lives of 3.3 days for ^{131}I and 15 days for ^{137}Cs, the figures for radionuclide ingestion of 270 Bq ^{131}I and 780 Bq ^{137}Cs are obtained. 80 Bq ^{131}I would be deposited in the thyroid, resulting in a thyroid committed dose equivalent of 0.12 mSv for an average Northern Ireland adult with a 20 g thyroid.[13] Radiocaesium ingestion would contribute a further 0.02 mSv[13] giving a total thyroid dose equivalent of 0.14 mSv. This figure is only 0.3% of the annual dose limit (50 mSv)[14] for the thyroids of members of the public, and may also be compared with a figure of approximately 1 mSv[15] for the population mean annual thyroid dose, which arises due to natural sources. The radiation doses to the thyroids of children would be several times greater, mainly due to the relative size of their thyroid glands[11] and other factors such as greater milk consumption. Ingestion of these radionuclides from milk would result in a committed effective dose equivalent of 0.024 mSv using standard conversion factors[13] for converting ingested radioactivity to effective dose equivalent.

Radiation doses have also been received by the Northern Ireland population from ingestion of radionuclides in other foods and from irradiation by external gamma rays from radioactivity deposited on the ground. Considerably smaller radiation doses have also been received from Chernobyl fall-out through other mechanisms including radionuclide inhalation, external irradiation from the passing Chernobyl cloud, and beta contamination on the skin. The National Radiological Protection Board have estimated the total effective dose equivalent to Northern Ireland

adults due to the Chernobyl cloud as 0.18 mSv over a lifetime.[16] This excess radiation dose to the whole body due to the Chernobyl accident represents less than one per cent of a typical dose of 76 mSv[17] which would be received by a Northern Ireland individual due to natural background radiation sources over a 40-year period.

From the measured thyroid activity of student A on 6 May (Table III), and making the pessimistic assumption that radionuclide ingestion occurred on 26 April, and allowing for ^{131}I decay, it is estimated that this student accumulated approximately 700 Bq (±50%) of ^{131}I in his thyroid within a few days of the accident. This is considerably greater than the estimated 80 Bq ^{131}I accumulated for a typical Northern Ireland adult within the month following the Chernobyl accident, clearly confirming that the population living within 100 km of Chernobyl was much more severely affected by the accident than the Northern Ireland population.

Student A was one of 99 UK students recalled by the Foreign and Commonwealth Office from the affected Minsk and Kiev regions around Chernobyl. Thyroid monitoring was performed at Heathrow airport by the National Radiological Protection Board[18] on these 99 students (in seven by a similar gamma ray spectrometry method applied in this investigation and in the remainder using a hand-held portable monitor). The NRPB estimated that the students' thyroids contained between 800 and 6900 Bq of ^{131}I at the time of measurement. Allowing for radioactive decay, student A's thyroid would have contained 550 Bq ^{131}I (±50%) and 84 Bq ^{137}Cs (±50%) when monitored at Heathrow, indicating that he was one of the least contaminated of the United Kingdom students evacuated from the USSR. The thyroid dose estimate for student A was 1 mSv, which represents 2% of the ICRP's annual dose limit for the thyroid of members of the public.[14] Student A was reassured that the radioactivity in his thyroid was well within recommended limits and need not be a matter for concern.

The finding that radionuclide contamination was below the levels of detection for the other three students is not unexpected in view of their large distance from Chernobyl, and since any ^{131}I in their thyroids would have decayed to approximately 1% in the intervening two-month period before measurement. While it is clearly difficult to attempt a precise dose estimate for these students so long after the accident, the negative findings indicate that radionuclide contamination for the students was not serious.

It is worth considering the long-term consequences of the Chernobyl fall-out on the health of the Northern Ireland population. All exposures to ionising radiations carry some risk of radiogenic cancers, which is the main concern in the present circumstances. The mean time for the appearance of radiogenic cancer is 20 years, and it is common practice to evaluate the risk of radiogenic cancer or death due to radiogenic cancer over a period of 40 years. The risk can be expressed numerically as the number of additional cancers or cancer deaths expected, if a population of one million is exposed to 10 mSv of radiation. For thyroid cancer, the risk is estimated at five cancer deaths and 100 non-fatal thyroid cancers per 10,000 man-sieverts to the thyroid,[14] while the risk for all cancers is 125–150 deaths per 10,000 man-sieverts to the whole body.[14, 19]

Assuming that milk consumption is the main contributor to thyroid dose, it would appear from the earlier estimates that the Northern Ireland population (1.57 million)[8] would have received a collective thyroid dose (see glossary) of the order of 200 to 300 man-sieverts. Based on this estimate and the risk factors, it appears

that there may be a small number of non-fatal thyroid cancers in Northern Ireland as a result of the Chernobyl fall-out. From the NRPB's most recent estimate of 0.18 mSv per person,[16] the Northern Ireland population would have received a collective whole body dose of about 300 man-sieverts. This would suggest a potential of three additional cancer deaths in Northern Ireland due to the Chernobyl accident over a period of 40 years, which may be compared with the 3290 cancer deaths which occurred in Northern Ireland in 1984,[20] giving a projected estimate of 100,000 over 40 years. Even this small number of additional cancer deaths might not all become manifest, since death could occur first due to other causes. Additional cancers due to Chernobyl in Northern Ireland will not be distinguishable from the much greater number of cancers due to other causes. It is evident from this comparison that the added risk to any individual is very small indeed and may best be judged in the context of the enormously greater risk of death due to potentially preventable diseases such as smoking-related lung cancer or coronary heart disease.[21]

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GLOSSARY

Physical half-life: The time taken for the number of atoms of a particular radionuclide in a sample to decay to half that number.

Biological half-life: The time taken for the number of atoms of a substance in an organ of the body to decrease to half that number, by biological excretion.

Effective half-life: The time taken for the level of a particular radionuclide in subsequent samples (e.g. thyroid or fresh milk) to decrease due to both physical decay and biological or natural removal processes.

Becquerel (Bq): The unit of measurement of radioactivity, equivalent to one nuclear transformation per second.

Committed dose equivalent: The radiation dose received over a lifetime by an organ from ingested radioactivity. Radiation dose equivalent and radiation dose have specific definitions, but for the present purposes have the same meaning.

Millisievert (mSv): The sievert (Sv) is the unit of measurement of radiation dose equivalent.

Committed effective dose equivalent (Whole body dose): Some organs and tissues of the body have a greater sensitivity to radiation than others. Calculation of the committed effective dose equivalent takes this into account by multiplying the committed dose equivalent for the organ by an appropriate weighting factor, and then adding the components for each organ to give the effective (whole body) dose. In a similar way, the radiation doses for each radionuclide are calculated separately and then summed to give the whole body dose.

Collective dose equivalent: The collective dose equivalent (expressed in man-sieverts) to a population is calculated by multiplying the population total by the mean dose equivalent per person. The collective dose equivalent may apply to the whole body or any specified organ.

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Needle biopsy of the pleura in the diagnosis of pleural effusion

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SUMMARY

Needle biopsy of the parietal pleura was undertaken in 64 patients with undiagnosed pleural effusion. An adequate specimen was obtained in 96% of procedures. This was diagnostic in 45% of those due to malignancy and in 50% of those due to tuberculosis. A second biopsy improved the combined diagnostic yield in these two diseases from 32% to 46%. Pleural fluid cytology was unhelpful in establishing the presence of a malignancy, and culture of the biopsy specimen was helpful in one case.

INTRODUCTION

Pleural disease is a common clinical problem. The pleural space may be involved in many diseases, and establishing a diagnosis may prove difficult. Needle biopsy of the parietal pleura was introduced by DeFrancis in 1955 and this proved to be an important advance.[1] There have since been a number of reports which have discussed the technique, indications, complications and diagnostic accuracy of closed pleural biopsy, with a comprehensive review by Light.[2] We report our experience of the diagnostic value of needle biopsy of the parietal pleura.

PATIENTS AND METHODS

The records of all patients with pleural effusion who underwent closed pleural biopsy between 1977 and 1984 using the Abrams needle were reviewed. Eighty-six biopsy procedures were performed on 64 patients with pleural effusion who had been admitted to the medical units of two hospitals which serve a population of approximately 160,000. Forty-one were male (mean age 61 years, range 21 to 85) and 23 female (mean age 57 years, range 16 to 87). At least three samples were submitted to routine histological examination at each procedure. The final diagnosis was established by evaluation of the results of pleural fluid analysis, histology of the pleural biopsy and of other sites, thoracotomy, autopsy and from the clinical course of the disease.

RESULTS

A single biopsy procedure was carried out on 47 patients (73%) and a second biopsy on 15 (23%). The remaining two patients had four and five biopsies respectively. An adequate specimen suitable for histological examination was

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obtained in 81 of 84 procedures (96%). The most common final diagnosis was malignancy in 31 patients (48%). In 20 patients (31%) the pleural effusion was associated with underlying pneumonia, and tuberculosis was diagnosed in six patients (9%). There were three patients with congestive cardiac failure and persistent pleural effusion which led to evaluation for coexistent pathology, all of whom eventually responded to diuretic therapy. Single cases of pleural involvement with rheumatoid disease, sarcoidosis and an empyema were found. No diagnosis was made in one patient lost to follow-up.

In the malignant group, out of a total of 31 patients, 14 had diagnostic histology and one was 'probable'. Fifteen showed non-specific fibrosis or inflammation, and no pleura was identified in one. The primary site was bronchus in 18 patients (58%), breast in three, ovary or uterus in two, gastrointestinal tract in two, lymphoma in two, prostate in one, and in three patients was unidentified.

Of the 20 patients in the para-pneumonic group, the biopsy specimen in 19 showed non-specific changes and in one no pleura was identified. All responded satisfactorily to antibiotic treatment. In the six patients with tuberculous effusion, three biopsies were positive and three showed non-specific fibrosis or inflammation. All these patients were Heaf positive grade 3 or 4, and subsequently had a satisfactory clinical and radiological response to anti-tuberculous treatment.

Seventeen patients had a second biopsy procedure. There were 10 in the malignant group, of whom four were diagnostic, and two in the tuberculous group, one being positive. The patient with sarcoidosis had four biopsies in close succession, the second being diagnostic. One patient, who had five biopsies, all of which proved negative, died of his primary abdominal neoplasm three months later. Pleural fluid was examined cytologically in 26 patients with a malignancy, but malignant cells were seen in only three cases (11%), and in two of these the pleural histology was also positive. Uniformly bloodstained fluid was found in 35% of those with malignancy, 20% of the para-pneumonic group, 50% of those with tuberculosis and in the patient with sarcoidosis. The procedure was well tolerated. Pneumothorax occurred after four procedures, one requiring tube drainage. Needle track seeding of tumour occurred in one patient.

DISCUSSION

Needle biopsy of the parietal pleura remains a useful and safe procedure in exudative effusion. No serious complications occurred. Pneumothoraces, large enough to require tube drainage, have been reported in about 1% of procedures[3-5] and there was a similar rate in our series. The overall complication rate was 6 per cent. Three patients with transudates due to congestive cardiac failure had biopsies performed at the time of diagnostic thoracocentesis, which might have been avoided by estimation of the pleural fluid content at the bedside, using a refractometer.[6] There had been a reversal in the incidence of the two most common causes of pleural exudates, tuberculosis and malignancy, since the introduction of closed pleural biopsy[5-9] and this was reflected in our findings of 48% malignant and 9% tuberculous causation.

The diagnostic return in malignant effusion compares favourably with that of previously reported series, 35–75% in malignant effusion.[10-13] In this study only 11% in this category had positive pleural fluid cytology, although the accuracy of cytological diagnosis has been reported as between 40% and 90%.[13, 14] The various factors contributing to an optimal yield include the tumour type, number of specimens examined, the methods of examination employed and the skill of

the cytologist.[2] In our experience, pleural biopsy was a much more reliable method of diagnosis than cytology, and this is likely to be the experience in other hospitals which do not have the services of a specialist cytologist. In the tuberculous group, 50% of biopsies were diagnostic, comparable to the yield of 38 to 71% in other series.[10-19] The diagnostic yield was increased by culture of one of the specimens.[16]

A second biopsy procedure was worthwhile, increasing the diagnostic yield in the tuberculous and malignancy groups combined from 32% to 46%. Similar results have been reported, with improvement in the specific diagnosis from 40% to 50% with a second biopsy.[10] Non-specific changes were seen in 48% of patients with malignancy in this study. This can be explained by the blind nature of the sampling technique employed, coupled with the patchy distribution of the disease on the pleura.[20] In addition, the pleura may not be directly involved, the effusion being caused by other mechanisms. Thoracoscopy has been advocated, especially in Europe, to overcome the problem of false negative biopsy, but at the expense of increased morbidity.[21]

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Case report

Primary torsion of the greater omentum

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Primary torsion of the greater omentum is a rare cause of acute abdominal pain. The diagnosis is rarely made before operation and most cases are diagnosed as acute appendicitis. I report a child with this condition and review eight other cases.

CASE HISTORY

A 10-year-old boy was admitted with pain in the right iliac fossa for two days, which was made worse by movement and coughing. He was not nauseated and he did not vomit. He had not eaten for two days. Pulse rate was 70 per min and temperature 37.4°C. There was marked tenderness with rebound in the right iliac fossa. On rectal examination he was very tender on the right side. White cell count was 8,300 per ml. A diagnosis of acute appendicitis was made. At operation a small piece of greater omentum which had undergone torsion was found lying directly beneath the incision. The twisted omentum measured 5 × 4 × 4 cm and formed part of the right lower quadrant of the greater omentum (Fig). The appendix was not inflamed. The terminal ileum appeared normal and a Meckel's diverticulum was not found. The piece of twisted omentum was ligated and excised and the appendix was removed. Histology revealed infarction of the greater omentum due to primary torsion and a normal appendix.

Fig. Infarcted right lower greater omentum.

Details of eight other cases of primary torsion of the greater omentum were collected from a search of the medical records at the Royal Victoria Hospital and the Belfast City Hospital over the past 20 years. Their ages ranged from three to 34 years (mean 17.5 years) and four were under 12 years old. All were males and one seven-year-old boy had Down's syndrome. All but one case was diagnosed as acute appendicitis. The average duration of symptoms before

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admission to hospital was two days. The most common presenting symptom was abdominal pain which was located in the right iliac fossa in five cases, on the right side of the abdomen in two and in the right hypochondrium in one. Other symptoms included nausea, vomiting, constipation and anorexia. Tenderness was located in the right iliac fossa in seven cases and was often accompanied by guarding and rebound. An abdominal mass was not palpable in any case. Only one had a temperature greater than 38°C and in only three was the white cell count elevated. In six cases a gridiron incision was used. There was free fluid in the peritoneal cavity in five which was bloodstained in three. All were found to have primary torsion of the greater omentum. The largest piece of omentum removed weighed 200g and the smallest weighed 5g. All recovered rapidly with minimal complications.

DISCUSSION

The first case of primary torsion of the greater omentum was reported by Eitel in 1899.[1] Primary or idiopathic torsion occurs in the absence of associated pathology.[2, 3] Secondary torsion which is more common may be associated with hernias, tumours, cysts or inflammation in the abdomen. Predisposing factors include obesity, a bifid omentum, tongue-like formations of omentum and omental malformations.[4] Payr suggested that redundancy of the veins in relation to the arterial supply caused kinking, with venous engorgement, the distended and tortuous veins rotating around the rigid arterial axis of the omentum, resulting in torsion.[5] It has been suggested that the onset is precipitated by trauma, over-eating, coughing, over-exertion, straining or an inflammatory focus.[6]

This group of cases includes five children, which is unusual, since primary torsion of the omentum is rare in childhood because the omentum is poorly developed and any twist will return immediately to normal. Primary torsion of the omentum affects all age groups but is most commonly seen in middle-aged men.[7] In two of the present cases, mesenteric adenitis was noted but this was not thought to be related to the torsion. In two there was a serosal reaction on the appendix which may have been secondary to the torsion. In another case the appendix exhibited a low-grade submucosal, subacute inflammation at its tip but it seems most unlikely that this could have caused the torsion. An uninflamed Meckel's diverticulum was found in two cases.

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Case report

Cardiac tamponade as a presenting symptom of bronchial carcinoma

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There are many causes of pericardial effusion. After excluding lymphoma and leukaemia, cardiac, metabolic, infective or immunological disorders take precedence to malignancies in the differential diagnosis. Clinical pericardial effusions are uncommon in patients with carcinoma of the bronchus, and cardiac tamponade as a presenting symptom is very rare. We report three such patients and relate them to the spectrum of bronchial carcinoma.

CASE HISTORIES

Patient 1: A 38-year-old female smoker presented at 28 weeks' gestation, with a two-week history of shortness of breath. On admission the jugular venous pressure was elevated and enlarged cervical lymph nodes were noted. Chest X-ray showed a lesion at the right hilum. Shortly afterwards, the patient spontaneously delivered a live female infant and then collapsed post-partum. Pulsus paradoxus and a systolic blood pressure of 90mmHg were noted. Echocardiography confirmed a large pericardial effusion with tamponade. Symptoms were relieved by aspiration of one litre of bloodstained fluid which contained dedifferentiated cells. Lymph node biopsy and bronchial brushings showed malignant cells in keeping with a large cell carcinoma. Despite one further pericardial aspiration and 2000 cgys radiotherapy over 11 days, she died 28 days after presentation.

Patient 2: This 44-year-old male smoker was admitted with a seven-week history of progressive dyspnoea, cough and mild weight loss. Admission blood pressure was 90/60mmHg with pulsus paradoxus and a positive Kussmaul's sign (a paradoxical rise in jugular venous pressure on inspiration). Enlarged, firm lymph nodes were present in the left supraclavicular fossa. Echocardiography demonstrated a pericardial effusion with tamponade. Computerised axial tomography showed a right lower lobe bronchial neoplasm with hilar node involvement. Aspiration of 700ml of bloodstained fluid, followed in 48 hours by a further 1800ml, temporarily relieved symptoms. Pericardial aspirates, sputum samples and lymph nodes contained adenocarcinoma cells. Despite local

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instillation of 500mg of tetracycline and 3500cgys radiotherapy over 19 days, he died 62 days after admission.

Patient 3: This 66-year-old male smoker presented with a three-month history of increasing dyspnoea. On examination blood pressure was 140/100mmHg and the venous pressure was elevated with marked pulsus paradoxus. Echocardiography demonstrated a pericardial effusion with tamponade. Computerised axial tomography showed a mass in the left lower lobe; 750ml of bloodstained pericardial fluid was aspirated. This and sputum samples contained adenocarcinoma cells. Despite instillation of 500mg tetracycline and 4000cgys radiotherapy over 30 days, the patient died 77 days after presentation.

DISCUSSION

In general, squamous cell tumours occur in 40 – 50% of reported series, small cell tumours in 22% and adenocarcinoma in 20%.[1] The male to female ratio is about 5:1. The relative incidence of adenocarcinoma may be increasing and accounts for 45% of bronchial tumours in women.[2] The incidence of squamous adenocarcinoma and small cell infiltrates of the pericardium is similar (10.5%, 11.7% and 9.5% respectively),[3] and where a pericardial effusion is present the incidence of adenocarcinoma is 66%, with a male to female ratio of less than 2:1.[4, 5]

Metastatic causes of pericardial effusion are not common.[6, 7, 8] The amount of fluid is variable and tamponade rare. A review of recent literature reveals a total of 49 patients with tamponade secondary to malignancy. Of these, 30 had a bronchial neoplasm, with a male to female ratio of 1.6:1.[6, 9, 10, 11]

The overall mean age of patients presenting with bronchial carcinoma is about 60 years.[9, 12] For squamous cell tumours, the mean age at presentation is 60 years with 12% of patients under the age of 50 years, for small cell tumours 55 years, with 30% under 50 years, and for adenocarcinoma 61 years.[13, 14, 15] In a large series of patients with adenocarcinoma and tamponade the mean age was 50.4 years with 52% under 54 years of age.[4] Thus patients with adenocarcinoma and tamponade are more likely to be young and female when compared with other patients with bronchogenic carcinoma.

The reason for this relatively young age at presentation is unclear. Increased local invasiveness with epicardial metastases may be a relevant factor.[16, 17] In patients with non-pulmonary carcinoma causing tamponade, the average age at presentation is 51 years which makes direct invasiveness unlikely to be the cause.

Tumour doubling time may be important. Adenocarcinoma has a slower doubling time (six months) than squamous carcinoma (three months) or small cell tumours (one month).[7] We postulate that the slow growth of adenocarcinoma cells in relatively young patients may lead to lymphatic obstruction and effusions, rather than the direct lymph node pressure effect of bronchial obstruction seen with more aggressive neoplasms.

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Case report

Therapeutic aspirin overdose in a three-year-old boy

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Multi-centre studies are in progress to clarify a possible association between Reye's syndrome and aspirin use by feverish children. In June 1986, the Committee on Safety of Medicines, in a letter to all doctors, announced that it had 'considered the available evidence and concluded that, while the causes of Reye's syndrome are not clearly defined, aspirin may be a contributory factor to the causation of Reye's syndrome in some children'. It considered it 'prudent to avoid giving aspirin to children under twelve years old unless specifically indicated'. Reye's syndrome is a rare acute encephalopathy associated with fatty change of the liver and occurring typically after viral infections. The clinical features may include vomiting and any degree of impaired consciousness.[1]

The following case history demonstrates that aspirin, when administered to children for straightforward febrile illness, even in the recommended dosage, can cause serious illness due to raised blood salicylate levels, quite apart from Reye's syndrome.

CASE HISTORY

A three-year-old boy was admitted to another hospital in April 1984 in a semi-conscious state. For four days he had been lethargic with a dry cough and decreased appetite. Three days prior to admission he had developed vomiting and pyrexia, for which his family doctor had prescribed 300 mg of acetylsalicylic acid three times daily. Twenty-four hours prior to admission the boy became drowsy with grunting respirations, and at 2.00 am on the morning of admission his parents found him in a stiffened position, with eyes rolling and teeth clenched, unresponsive to their voices.

On admission he was clinically dehydrated with rapid, grunting respirations. His breath smelt ketotic. He was unresponsive to non-painful stimuli. His pupils were of normal size and reacted sluggishly to light. There was generalised hypotonia. Blood sampling revealed a relative lymphocytosis, metabolic acidosis, normal blood sugar, normal liver function tests, increased prothrombin time and normal serum ammonia. Blood salicylate level was 537 mg/l (forced alkaline diuresis is normally indicated at levels of greater than 350 mg/l). Chest X-ray was clear and cultures of blood, cerebrospinal fluid and urine were to prove sterile.

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The boy's stomach was washed out, intramuscular vitamin K_1 was administered and intravenous 4.5% sodium bicarbonate and diuretics were commenced. Seventeen hours following admission the urinary pH had risen to 7.0. The intravenous infusion was changed to 0.18% sodium chloride, 4% dextrose and potassium supplements. Twenty-four hours following admission his condition had deteriorated. His pupils were dilated but still reacting to light, blood pressure was raised and there was early papilloedema. 30ml of 20% mannitol were administered intravenously and fluid input was restricted. Crepitations were audible at both lung bases and chest X-ray showed early pulmonary oedema. Additional intravenous frusemide was administered and transfer to the Royal Belfast Hospital for Sick Children was arranged. Before transport arrived, the boy's temperature rose to 39°C and he suffered a three-minute generalised seizure, treated successfully with intravenous diazepam. On arrival at the Royal Belfast Hospital for Sick Children intensive care unit a further convulsion required intravenous diazepam and phenytoin, and endotracheal intubation followed by intermittent positive pressure ventilation for subsequent cyanosis and decreased consciousness. Ventilatory requirements were low and extubation was possible 48 hours later. He was later transferred back to the referring hospital where diuretics were stopped on the thirteenth day after first admission. Phenytoin was discontinued two months after discharge. There have been no further fits and both physical and developmental follow-up since have been normal.

DISCUSSION

In 1974, of a total of six cases of aspirin overdose admitted to the Royal Belfast Hospital for Sick Children, three were accidental and three therapeutic. This picture changed rapidly as a result of the introduction of child-resistant containers in 1976,[2,3] smaller pack sizes and attempts to eliminate attractively-coloured tablets. A review of admissions in a one-year period a decade later revealed five cases of aspirin poisoning, all of whom had had the drug either prescribed by a medical practitioner or given to them by their parents without medical advice. With only one exception aspirin had been administered in the recommended dosage for age. Despite this the five patients' blood salicylate levels ranged from 300 to 600mg/l and all required (at least) forced alkaline diuresis. Aspirin is poorly soluble in the acid solution in the stomach and may precipitate out, forming a coating on the stomach wall from which slow absorption can take place. This underlines the importance of stomach washouts as soon as possible after ingestion of large amounts of aspirin.

Salicylates directly stimulate the respiratory centre causing a respiratory alkalosis and a compensatory metabolic acidosis. They alter the function of the Krebs cycle to bring about an accumulation of lactate and decouple oxidative phosphorylation so that energy is wasted as hyperpyrexia. Bleeding may result from local gastro-intestinal irritation, altered platelet function or defective prothrombin synthesis. Hypokalaemia may be due to a direct effect on the renal tubular mechanism, or indirectly from the respiratory alkalosis. Hypoglycaemia or hyperglycaemia may occur, the former is the more serious clinically. In general, the three cardinal symptoms are vomiting, hyperventilation and hyperthermia, and aspirin poisoning should always be considered when these coincide in a child.[4,5]

There has been much debate about a possible association between Reye's syndrome and aspirin.[6] The connection does not appear to be dose-related[7] but the ages of children who suffer from Reye's syndrome during influenza epidemics

have been found to correlate more closely with the age distribution of aspirin use than with that of influenza.[8, 9, 10] Involvement of the central nervous system[11] and liver[12, 13] occurs both in aspirin overdose and Reye's syndrome and parallels have been drawn between the various toxic metabolites which accumulate in both conditions.[14, 15]

If there is a causal relationship between aspirin and Reye's syndrome, there should be a decline in cases as aspirin use is restricted. However, epidemic rates of the viral illnesses which precede Reye's syndrome may change, and the rate of reporting of Reye's syndrome by physicians may increase as more doctors become aware of it.[16] In any case, Reye's syndrome or not, the preceding history demonstrates that the decision to limit the use of aspirin for simple febrile childhood illnesses has been a wise one.

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Case report

Non-union of fracture of the carpal scaphoid in a child

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Complications arising from fractures of the scaphoid in children are exceedingly rare. Southcott and Rosman reported the only series of non-union of the scaphoid, eight cases occurring over a seven-year period at the Montreal Children's Hospital.[1] In their series, all the fractures occurred through the waist of the scaphoid and all ultimately required bone grafting. Only one of their patients was under 10 at the time of injury. This report represents only the second published case of non-union in a child under the age of 10 years.

CASE HISTORY

In October 1984, a nine-year-old boy attended the casualty department with a history of having fallen on his outstretched left hand. He was found to be tender over the dorsum of the wrist, with marked swelling and restriction of movement. The initial radiograph (Fig 1) revealed a fracture of the waist of the scaphoid. A scaphoid-type plaster was applied and immobilisation maintained for a period of five weeks. On removal of the plaster cast, a further X-ray (Fig 2) revealed the scaphoid to be a little more sclerotic than the surrounding carpal bones and the fracture line to be clearly visible. Three weeks later, the sclerosis was more definite (Fig 3), consistent with avascular necrosis. An X-ray four months from injury revealed some cystic changes at the fracture site with no evidence of bony union (Fig 4). At 11 months from injury, the radiograph showed the signs of established non-union (Fig 5), with marked cystic change and sclerosis on either side of the fracture site. Clinically, the patient was virtually asymptomatic and he remains so, more than two years from injury.

DISCUSSION

The relatively thick layer of cartilage which surrounds the carpal bones of children makes fracture of the scaphoid or any of the other carpal bones rare when compared with the incidence in adults. In adults, scaphoid fractures evoke particular interest because of their reputation for avascular necrosis and non-union. Several series attest to the relative rarity of this injury in children.[2, 3] In children under the age of 15 years, fractures of the distal end of the radius are the most common upper limb fracture. Blount[4] and Sharrard[5] refer only briefly to

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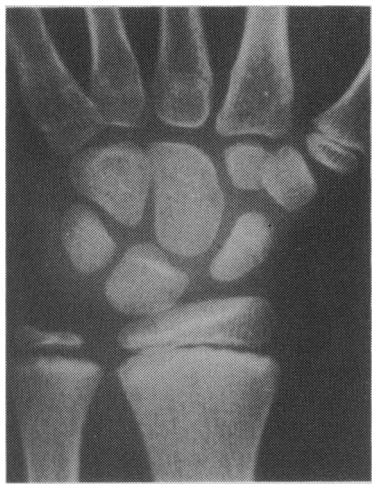
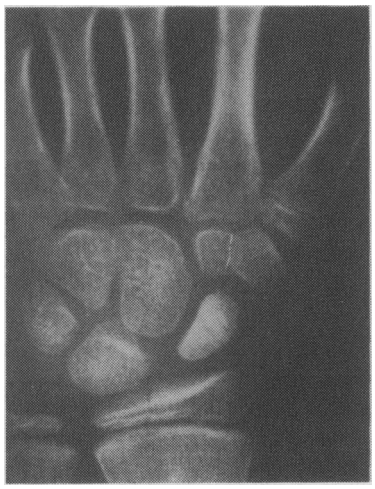
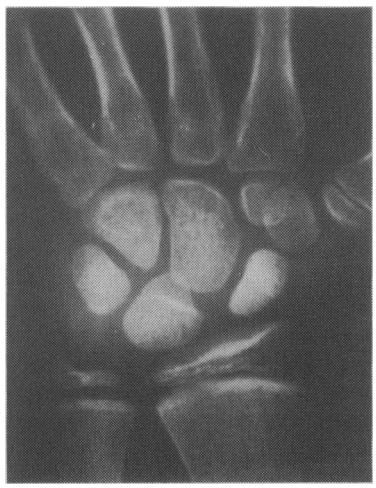
(Fig 1)



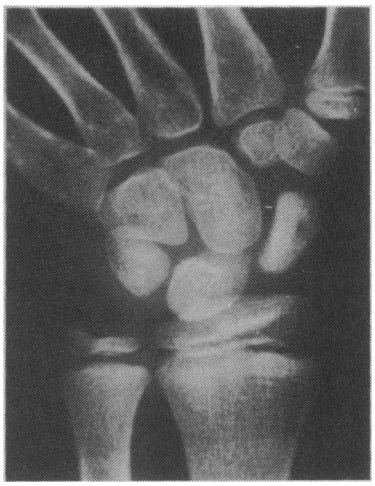
(Fig 2)



(Fig 3)



(Fig 4)



(Fig 5)

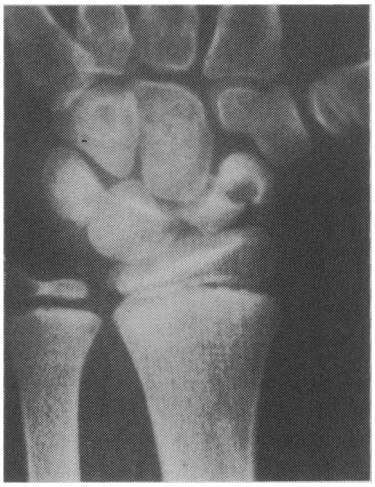


Fig 1. Radiograph taken on the day of injury. Note the undisplaced fracture of the waist of the scaphoid.

Fig 2. At five weeks the fracture line is still visible and the scaphoid is a little more sclerotic than the surrounding carpal bones.

Fig 3. X-ray at eight weeks from injury demonstrates increased sclerosis of the scaphoid. The appearance was, at this stage, reported as being consistent with avascular necrosis.

Fig 4. At four months, the fracture line has reappeared and cystic change is becoming evident.

Fig 5. Eleven months from injury the radiological signs of non-union are present, i.e. cyst formation and sclerosis on either side of the fracture line.

injury to the scaphoid, without mention of the non-union, and other standard texts omit all mention of scaphoid fractures in children.[6, 7]

Several distinct differences exist between scaphoid fractures in children and in adults. Proximal pole fractures, which are most commonly complicated by non-union, are almost never seen in children.[8] The distal pole, rather than the waist, is the commonest fracture site in children and this is often a manifestation of an associated ligamentous injury. These injuries heal readily with immobilisation in plaster. The blood supply to the scaphoid is similar in children and in adults, and fractures of the waist would endanger the vascularity of the proximal pole, producing avascular necrosis and non-union.[9] Failure to diagnose the original injury and institute correct treatment is a prime cause of complications. Swelling over the dorsal aspect of the radio-carpal joint and especially obliteration of the anatomical snuffbox should alert the clinician to the possibility of this particular injury. Attention should be directed to the scaphoid when no fracture of the distal radius is radiologically apparent.

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Case report

Infectious mononucleosis with cranial nerve palsies

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Accepted 2 October 1986.

The neurological complications of infectious mononucleosis may rarely occur in the absence of the classical symptoms and signs of infectious mononucleosis. Widespread involvement of the cranial nerves is very rare. It is important to consider infectious mononucleosis in the differential diagnosis of any young adult presenting with a neurological illness.

CASE HISTORY

A 19-year-old female student presented with a one-week history of headaches in the left temple, each lasting two hours and preceding a sudden onset of diplopia and left ptosis, which came on while she was photocopying at work. The diplopia deteriorated over the next few days and she developed an aching pain in the jaw. There was a three-day history of difficulty in swallowing and of slurring of speech. In particular, she had difficulty moving food around her mouth. There was no history of weakness in the limbs. She had had a mild irritation of her throat two or three weeks prior to her admission. There was no history of fever. She was well nourished, alert and well orientated. There was no significant enlargement or tenderness of the lymph nodes. She was not icteric. There were no rashes. She was normotensive, in sinus rhythm and had no cardiac murmurs. The chest was clinically clear. Liver and spleen were not palpable.

The pupils were normal size and reacted normally to light and accommodation. Visual acuity was 6/6 on both sides. Fields of vision were full. Optic fundi were normal. There was no bilateral ptosis. External ocular movements were restricted on both sides. Depression and adduction were full in both eyes. In the right eye, adduction was reduced to 50% of the full range and elevation to 25%. In the left eye, elevation was reduced to 50% and adduction to 75%. There was no nystagmus. Corneal reflexes and facial sensation were normal. Jaw jerk was not present. There was no wasting or weakness of the jaw muscles. There was an almost complete bilateral facial palsy. Hearing was not impaired and she could hear a whisper at two feet. Rinnie's and Weber's tests were normal. The soft palate moved normally, and gag reflexes were normal. The sternomastoids and trapezii had full power. The tongue was weak and could not be protruded fully. It

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could not be placed in either cheek. In the limbs, the power tone and co-ordination were normal. The tendon reflexes were all present, equal and normal. The plantar responses were flexor. There was no limb ataxia. There was no sensory loss. Tensilon test was negative.

The monospot test was positive, and the Paul-Bunnell reaction positive to a titre of 512, with absorption by ox cells but not by guinea pig cells. Epstein-Barr virus specific IgM was present in the serum, and about three months after the onset of her illness antibody to Epstein-Barr nuclear antigen was detected. Haemoglobin concentration was 12.5 g/l, with normal red cell indices. White cell count was 6,500/ml, with an excess of abnormal mononuclear cells. Chest X-ray was normal, CT scan of skull normal, EEG normal. Cerebrospinal fluid protein 0.30 g/l red cells <1 per µl lymphocytes 5 per µl. Serum sodium was 141 mmol/l, potassium 4.0 mmol/l, urea 3.6 mmol/l, total protein 82 g/l, albumin 45 g/l. Liver function tests showed total bilirubin 4 µmol/l, alkaline phosphatase 138 U/l, lactic dehydrogenase 303 U/l (normal range 130-270), aspartate transaminase 72 U/l, alanine transaminase 198 U/l, gamma glutamyl transpeptidase 43 U/l (normal 5-34), pseudocholinesterase 103 U/l. Prothrombin time was 62%. HBs Ag was negative, antinuclear factor negative, antistriated muscle antibody negative. Nerve conduction studies were normal in the right median and lateral popliteal nerves. (The usual range is quoted in brackets only where the value obtained was abnormal).

Following admission there was no deterioration in her condition. She was started on prednisolone 60 mg and this was tailed off over 10 days. It made no impression on her palsies, which slowly improved over a period of three months. At recent review she was symptom-free and had no sequelae.

COMMENT

The neurological complications of infectious mononucleosis were first reported in 1931.[1,2] The range of complications includes meningitis, encephalitis, cranial nerve lesions, mononeuritis, polyneuritis and spinal cord lesions; transient psychotic episodes have also been reported.[3,4] The incidence of neurological complications is difficult to assess, because many series are based on hospital patients and thus tend to include the more severe cases of infectious mononucleosis; however, it has been reported as varying from 0.37% to 26.5%.[5]

The neurological involvement can precede or follow the common manifestations of fever, pharyngitis, lymphadenopathy and splenomegaly, and in some cases the only clinical signs of infectious mononucleosis have been related to the nervous system.[5] All the cranial nerves have been involved in the disease,[4] although multiple involvement of cranial nerves, as in this case, is rare.[6] We have found only one case reported in the literature where the range of cranial nerve involvement was so widespread.[3] The Miller Fisher syndrome (ophthalmoplegia, ataxia and areflexia) has been reported in association with infectious mononucleosis[8] but does not satisfactorily describe this case. The pathological changes in the brain in patients dying with signs of cerebral damage consist of inflammatory lesions with dense perivascular cuffing and diffuse infiltration of the parenchyema mainly with atypical mononuclear cells.[7]

The prognosis is good for a complete recovery of the neurological complications.[5] In the cases involving the cranial nerves, the mean time to complete recovery was 70 days with a range of two to 240 days.[6] The use of steroids is controversial. Some authors recommend that steroids should be used in cases where infectious

mononucleosis is complicated by neurological involvement,[9, 10] but there does not seem to be good evidence that their use is beneficial.[6] There is also the consideration that steroids may enhance replication of herpes viruses.

We are grateful to Dr J H Connolly of the Northern Ireland Virus Reference Laboratory for performing the confirmatory tests. We also thank Mrs Dorothy Boyle for typing the manuscript.

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Case report

Malignant melanoma in pregnancy

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Accepted 19 January 1987.

Malignant melanoma is an increasingly common condition in young women.[1] If pregnancy occurs, the prognosis for the tumour may be adversely affected. Clinicians should be constantly aware of these tumours and the possible effect on prognosis by a concurrent pregnancy.

CASE HISTORY

A 32-year-old primagravida with no significant past medical history attended for booking at 13 weeks' amenorrhoea. She had used a combined oral contraceptive pill for four years until approximately six months prior to conception. She smoked 10 cigarettes per day. She received shared antenatal care which was uneventful until the spontaneous onset of labour at 38 weeks' gestation. After a seven-hour labour with epidural anaesthesia she had a vacuum extraction of a live male infant weighing 2835 g. On the first day of the puerperium, routine examination of the patient revealed a 1-cm-diameter pigmented lesion on the lateral aspect of the left lower calf. On further enquiry this lesion had been present for many years but during the pregnancy it had enlarged slightly. There was no associated irritation, pain nor bleeding. This lesion was clinically suspicious of a malignant melanoma. There was no lymphadenopathy, hepatomegaly nor bony tenderness and the lung fields were clinically normal.

On the fourth post-partum day, excisional biopsy was carried out under general anaesthesia, and histology revealed a malignant melanoma. On the sixth post-partum day, the site of the lesion was widely excised and the defect covered by a split skin graft from the right thigh. Prophylactic heparin, 5000 IU twice daily, was administered until the patient was fully mobile. Histological examination revealed a malignant melanoma 0.5 cm × 0.75 cm with no spread within the limits of the specimen. The tumour extended to the level of the recticular dermis corresponding to Clarke Level 3. Chest X-ray, liver function tests and biochemical bone profile were all normal. Prophylactic groin lymph node biopsy was not performed but computerised tomography of the groin and pelvic lymph nodes was normal. The placenta was disposed of prior to the diagnosis of melanoma and, though macroscopically normal, was not subjected to histological examination.

DISCUSSION

During pregnancy, melatonin (MSH) is markedly raised, leading to the well-known pigmentation of pregnancy. However, the effect of pregnancy on a

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pre-existing melanoma is not clear, with conflicting evidence in the literature. Houghton has shown no significant alteration in the prognosis,[2] whereas Shiu found a significant worsening due to pregnancy only in Stage II disease where regional lymph nodes were involved.[3] Eleven studies were reviewed in detail by Holly, who found overall no survival difference related to pregnancy in females with malignant melanoma.[4] In fact, Hersey et al demonstrated a better survival in parous women when compared with nulliparous controls.[5] Treatment of malignant melanoma remains primarily surgical, which in pregnancy is complicated by the risks of deep vein thrombosis and aspiration pneumonitis if general anaesthesia is used. Hormone manipulation, termination of pregnancy, oophorectomy, adrenalectomy and hypophysectomy have not been shown to be of any benefit. Freedman and MacMahon have shown that metastasis to the placenta and the fetus, fortunately, is rare.[6]

With regard to future pregnancies, Shiu would discourage pregnancy in patients with a history of Stage II disease or those with previous activation of the lesion during pregnancy.[3] Recent reviews of this literature conclude that subsequent pregnancy has little if any adverse effect upon recurrence or survival rates.[7, 8] Finally, should these patients use combined oral contraceptives because of the possible adverse effects of any oestrogen components? Early reports were conflicting, and recent case control studies[9] have shown no increase in risk with combined oral contraception, suggesting there may be a protective effect in some age groups. There is no advice available on the use of progesterone only contraceptive medication.

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Case report

Recurrent vulvo-vaginal ulceration — Behçet's syndrome

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Accepted 20 January 1987.

Behçet's syndrome is a rare disorder described in 1937 by Hulusi Behçet, a Turkish dermatologist, as the triad of recurrent oral ulceration, genital ulceration and iritis.[1] It is a multisystem disease[2] with no pathognomonic clinical signs, diagnostic investigations or pathological findings.

CASE HISTORY

A 15-year-old girl presented to the Ulster Hospital with a painful vulvo-vaginal sore. She was not sexually active. There was an indurated ulcer at the posterior fourchette. Her temperature was 37.4°C, there was a polymorph leucocytosis, and ESR was 33 mm/hr. The lesion was excised; histopathology showed non-specific inflammation.

She later presented to the Samaritan Hospital, Belfast. The lesion had recurred and spontaneously resolved on three occasions, and she had had recurrent 'cold sores' on the lips, 'sores inside the mouth' and 'red eyes'. Her temperature was 38.3°C; there was ulceration of the buccal mucosa and a tender ulcer at the posterior fourchette. Eye examination was normal. Investigations showed a polymorph leucocytosis and ESR 38 mm/hr. Serological tests for syphilis were negative (VDRL and TPHA). Throat, vaginal, urethral and endocervical swabs showed no growth. Histopathology of the vulval lesion showed an intensely vascular response with perivascular cuffing of chronic inflammatory cells.

She then developed generalised arthralgia, with tender swelling of the left ankle and left knee joints, and had a marked systemic upset. The ESR was now 60 mm/hr, white cell count 15×10^9/l, C-reactive protein 21 mg/l (normal < 6 mg/l), alpha-1 and alpha-2 globulin fractions slightly raised. Serological tests and routine thyroid and rheumatological autoantibody tests were normal. X-rays of chest, the affected joints and the sacroiliac joints were all normal. The aspirate from the left knee showed a few polymorphs but was sterile on culture. The mouth ulcers and joint problems continue to recur, and the left knee joint requires periodic aspiration. She is currently treated with non-steroidal anti-inflammatory agents. A microcytic hypochromic anaemia and elevated ESR (46 – 81 mm/hr) persist.

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DISCUSSION

An incomplete survey of known cases of Behçet's syndrome in Northern Ireland was obtained by postal enquiry with all consultant gynaecologists, and by personal enquiry at referral centres for ophthalmology, genito-urinary medicine, dermatology and rheumatology. The medical records of departments of the larger hospitals in Northern Ireland were also requested to identify cases from their diagnostic lists. From this enquiry 13 other cases were identified, 10 female and three male, with an average age of about 25 years. The majority had presented with oral or genital lesions; joint, skin or eye lesions were less common at onset. Four had considerable general malaise, and several had had symptoms for several years before the diagnosis was established.

Major complications encountered in this group included severe visual loss in four, progressive joint disease in four, inflammatory bowel disease in three, and depressive illness in three. Other problems included aseptic meningitis, recurrent thrombophlebitis, pulmonary hypertension from recurrent infarction, and peripheral neuropathy. Treatment offered had been variable, most commonly corticosteroids, and response in general poor. No mortality occurred due to the disorder, but four patients were severely handicapped. Two had become pregnant.

The present case illustrates that the diagnosis, though often delayed, is essentially clinical. The relapses and remissions and mainly negative results help to exclude other diseases. The typical histopathology is an intense vasculitis mainly involving the venules. Behçet grouped together recurrent eye, oral and genital lesions although Hippocrates may have been the first to describe such affliction.[3] The syndrome, however, has protean manifestations. Other features include pathergy (hyper-irritability of the skin), gastrointestinal lesions, and vascular involvement causing peripheral vascular disease and portal hypertension. Joint involvement is typically mono-articular, the knee being the commonest site, and the sacroiliac joints are rarely involved. Radiological appearances of the joints are normal and any effusion is sterile.[2] It is regarded as an oculomucocutaneous disorder, other variants being Reiter's disease and erythema multiforme. Ocular involvement is said to cause most morbidity and vascular involvement most mortality.[2] Prognosis is guarded, but early age of onset, male sex, frequent recurrences and early vascular involvement indicate a poor prognosis. An overall mortality of 3–4% has been reported in Japan.[2]

The syndrome has a worldwide distribution, and is most prevalent in Turkey, the Middle East and Japan. Chamberlain found a prevalence of 0.6 per 100,000 in England,[4] and the 14 cases reported here would represent 0.9 per 100,000 in Northern Ireland. It is slightly more common in males. The aetiology remains unknown.[5] Behçet favoured a viral aetiology but recent studies are inconclusive.[6] Immunological mechanisms have been proposed but the documented immunological changes are often transient, appear only during relapses and are non-specific. They may be found in patients with recurrent oral ulceration who never develop Behçet's syndrome. Immune complexes have been found in the circulation and at sites of disease[7] and non-specific autoantibodies have also been found.

In pregnancy, the spontaneous abortion and congenital malformation rates are unaffected. Seriously ill patients may be infertile, but may also conceive while on treatment, and there may be a temporary remission in pregnancy.[8] Transient

mucocutaneous lesions have been found on some neonates whose mothers have the disease.[9] One aborted fetus had an aortitis typical of that reported in Behçet's syndrome.[10] Treatment is unsatisfactory and corticosteroids still remain the treatment of choice, but these and other drugs including immunosuppressive agents are not without risk.

I wish to thank Mr J K Houston, Consultant Gynaecologist, Samaritan Hospital, for permission to report this patient. Also Dr R Maw, Department of Genito-Urinary Medicine, Royal Victoria Hospital, and Dr A Taggart, Department of Therapeutics and Pharmacology, The Queen's University of Belfast, for their comments and advice, and Miss May Weller for typing the manuscript.

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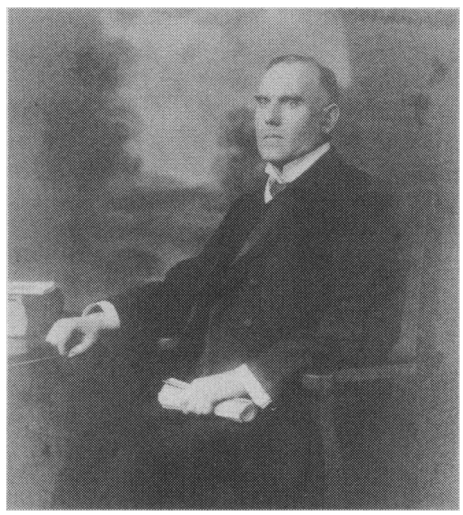
Historical Note

Duodenal ulcer, hyperacidity and J C Adams

T L Kennedy

Accepted 6 February 1987.

Every medical student knows that duodenal ulcer is usually associated with hyperacidity and the cogniscenti believe that it was Lord Moynihan who first made this observation. We are indebted to Dr Hugh Baron for pointing out that the credit is, in fact, due to James Cowan Adams.[1]



Dr J C Adams (1871-1951), at the time of the award of his MD degree, 15 July 1911.

It was in 1911 that Adams submitted his MD thesis to the Queen's University of Belfast. Regrettably, the original has now disappeared, but Baron was able to read it in 1969 and now tells us that Adams had carefully studied 20 patients with proven duodenal ulcer. Fourteen of these, including many with pyloric stenosis, had hyperchlorhydria on the evidence of Ewald test meals. Hence Moynihan's much quoted figure of 70% for duodenal ulcer patients with hyperacidity.[2] Adams then wrote 'Hyperchlorhydria . . . is a condition of congestion, hyperaesthesia and hyper-acidity . . . with intervals between attacks . . . It might be that after this condition had existed for some length of time an ulcer formed. In some cases there is a continuous and copious flow of saliva which is very distressing to the patient'. Adams had thus taken much further the classic observation of Schwarz — 'no acid, no ulcer'.[3] It was about this time that A B Mitchell published an account of a series of nine operations for perforated duodenal ulcer carried out between 1904 and 1908 at the Royal Victoria Hospital, Belfast, with no deaths — a remarkable achievement at that time.[4] The first vagotomy in man was done by Exner in Germany in 1911, but the indication was to relieve the pain of tabetic crisis, not for duodenal ulcer.

Adams came from a family of County Antrim farmers and graduated from Queen's College in 1888. He spent the rest of his life in general practice at 212 Ravenhill Road, Belfast. He travelled widely to hospitals in both Europe and North America. Our present-day MD and PhD candidates will be surprised to learn that

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he took no time off from his practice for his research. He did the work mostly at night. There were no Eastern Board or Royal Victoria Hospital Fellowships in those days! Many of his family have followed him into medicine and remember his as 'large, straight and rather stern'. Sir Ian Fraser describes him as big, burly, jovial and friendly. Perhaps he was a modest man, as he never published his work in any journal, or perhaps it was just that *curricula vitae* were not important in his time.

I am greatly indebted to Dr Hugh Baron for giving us this information and for his permission to quote freely from his paper. The photograph of her grandfather was supplied by Dr Sandra Redmond, Broughshane, Co Antrim.

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BOOK REVIEW

A guide to radiological procedures. By Stephen Chapman and Richard Nakielny. 2nd ed. (pp 274. £8.95). London: Baillière Tindall, 1986.

It is a pleasure to recommend the second edition of this book. I can only repeat what I have said about the first edition — that it represents excellent value for money. I think the authors are to be congratulated on the content and presentation, and their bravery in publishing a book on techniques should not be under-estimated, as virtually every radiologist has an individual approach to each examination. It is extremely difficult for the young radiologist to assemble all the basic information required in radiological procedures and the authors have managed to present this material in a form which will be useful to both trainees and senior staff.

One must, however, enter some minor caveats. The fact that iron deficiency anaemia is not mentioned as an indication for barium enema examination is surprising. Many radiologists would not recommend puncture of the posterior wall of the femoral artery as being a routine part of the Seldinger technique, and I find it surprising that various contrast media are recommended by their trade rather than their generic names. Some of the examinations included are virtually obsolete, such as gynaecography, for demonstration of the ovaries, and Myodil meatography, for acoustic neuroma, but to balance this the inclusion of indications for computed tomography and nuclear magnetic resonance imaging is to be welcomed. Ultrasound techniques are outside the remit of this work.

All in all, this is an excellent book. Obviously, if it is used by trainees in the context of the requirements of their own departments, it will prove to be of great value. It can be, therefore, highly recommended.

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