patients has considerable cost consequences for the NHS.

Chest pain units, first developed in the United States, attempt to improve diagnostic accuracy, shorten length of hospital stay, and save money.[9] Such units take patients who have already had a full history, examination, and ECG and do not have an acute coronary syndrome and have been assessed to be at low or moderate risk. Usually these units are located within emergency departments and are protocol driven. Typically, patients are closely monitored for 6-12 hours, subjected to a battery of biochemical tests, serial ECGs, and often ST segment monitoring and an exercise ECG. If all these tests are negative the patient is sent home, but if tests are positive or equivocal the patient is admitted for further investigation and treatment. However, the units vary in their selection criteria, length of observation, use of cardiac tests, and discharge criteria.

Have chest pain units led to any improvement in diagnostic accuracy and clinical outcome? Most of the evidence comes from North America and shows that chest pain units are safe, with no significant difference in event rate, reattendance, or readmission rate compared with conventional care.[10] However, these studies were not sufficiently powered to show improvement in rare events (mortality of patients inadvertently sent home), and in many studies all those who served as controls were admitted. Diagnostic certainty was increased and length of stay reduced. The economic analyses are predominantly North American and suggest modest savings. Often the economic perspective taken is departmental rather than from a healthcare system or societal perspective. Whether such savings would be made in the United Kingdom with its very different practices (much less interventional radiology, and higher discharge rates from emergency departments) is uncertain: there is little evidence to guide us.

In the United Kingdom a small but increasing number of emergency departments are running chest pain units, and the limited evidence available of their diagnostic performance is encouraging.[11] These are very different from the new and more common chest pain clinics, which deal with patients judged by their primary care practitioner not to require emergency care. Patients are seen by cardiologists and may undergo provocative cardiac testing, but the clinics do not usually provide observation and biochemical testing.

The government's focus on coronary heart disease, with its recommendation that patients or their doctors call for an ambulance in the event of symptoms that suggest acute myocardial infarction,[12] make it almost certain that the large numbers of patients with chest pain currently seen in emergency departments will increase. If the patient group is to be dealt with safely and efficiently then practice will need to change. The difficulty is that the problem is already here and getting worse, and the ideal evidence from a UK multicentre randomised controlled trial is absent. We have to decide urgently whether the systematic approach to the diagnosis of chest pain in those patients who present as emergencies, such as the approach offered by chest pain units, is likely to be better than existing care. If the answer is yes then the investment in such units is needed. A method of dealing with the growing wave of patients with chest pain in emergency departments is needed. Otherwise, the wards will be swamped with patients who do not need to be there, and as the pressure to avoid admission inexorably rises, so will rates of inappropriate discharge from emergency departments.

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Health risks in babies born after assisted reproduction

Risk of anomalies, low birth weight, and multiple pregnancies may be increased

Parents who conceive after fertility treatments would like to know if their children are at excess health risks compared with children who have been conceived naturally. They would like studies to be done to monitor outcome—but not necessarily on their own children.

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Outcome studies of in vitro fertilisation are relatively few to date and hampered by difficulties such as high cost, ethical considerations, recruitment of appropriate controls, and unwillingness of some parents even to tell their children how they were conceived, let alone bring them for assessments. Early

studies were small, uncontrolled, and had other methodological errors. In contrast the pace of advances in the treatment of infertility has been rapid. The development of embryo cryopreservation has been followed by potentially more hazardous techniques such as intracytoplasmic sperm injection and extended embryo culture. Other techniques entail manipulating the embryo in vitro by assisted hatching and preimplantation genetic diagnosis, a diagnostic procedure.

The eldest individuals born after in vitro fertilisation are now young adults, and 1% of children in developed countries are now conceived through in vitro fertilisation. Ultimately when this first generation of children born after in vitro fertilisation grow up, they will become a sizeable subgroup of the population. It is therefore regrettable that it has taken 20 years before an attempt was made to quantify the risk of congenital anomalies to children conceived by in vitro fertilisation.[1] Other recent studies investigating this risk after a more invasive method—intracytoplasmic sperm injection—include the reassuring series by Bonduelle, which quantified risk only in comparison with babies conceived by in vitro fertilisation but not with babies conceived naturally.[2] This series did not adjust for the inclusion of babies born after pregnancies achieved with different hormonal regimens or take into consideration that intracytoplasmic sperm injection sometimes involved non-ejaculated sperm. More recently a report by Hansen et al found an increased risk of anomalies in babies conceived after intracytoplasmic sperm injection, but this study was weakened by efforts to avoid observational bias by relying solely on one blinded paediatrician to determine whether congenital anomalies observed were more likely in babies conceived after this procedure.[3]

In vitro fertilisation carries an increased risk of higher order births with their attendant risk of major morbidity. Some countries have made efforts to limit replacement of embryos to two (Australia, New Zealand) or even one (Sweden, Finland), whereas other countries have not, despite clear evidence that replacement of three embryos increases only the risk of the birth of triplets but not the overall pregnancy rate.[4] The frequency of higher order births (three or more) between 1973 and 1990 increased at about seven times that of singleton births, and, whereas higher order multiple births represented only 1.6% of all births in 1973, they accounted for 3.1% of all multiple births in 1990 in the United States.[5] In the United Kingdom, comments by a former chairman of the Human Fertilisation and Embryology Authority have suggested that clinics responsible for the births of triplets due to replacing three or more embryos should contribute to their excess costs of care on the NHS. Couples who have waited many years to conceive may not believe the counsellor when told of a risk of triplets because the chance of having any baby seems so remote.

Other critical issues seem to be the risk of higher perinatal morbidity (related largely to complications of multiple pregnancy), the longer term risk of neurodevelopmental disadvantage, and the postulated risk of the in vitro environment causing an increase of diseases affected by genomic imprinting, such as Beckwith-Wiedemann syndrome or cancers such as osteosarcoma. Whether children born after in vitro fertilisation have normal fertility will be a sensitive issue to investigate.

Published studies on young children conceived after in vitro fertilisation, embryo cryopreservation, and intracytoplasmic sperm injection have been generally reassuring.[6–8] A report from the United States seems to confirm that, by itself, singletons born after in vitro fertilisation are lighter than their naturally conceived peers.[9] Before this it was always assumed that the lower birth weights were an effect of the 20-30% rise in higher order births in this population. Another study from Sweden suggests that higher risks of cerebral palsy are not just due to the increase in multiple births.[10]

No meaningful studies have investigated the effects of preimplantation genetic diagnosis beyond the neonatal period, although the technique entails major manipulation of embryos by the removal of one or two cells from the embryo at the eight to 10 cell stage (up to 25% of the cell mass). The newer techniques, however, such as transfusion of ooplasm, are not yet addressable (the numbers are too small) and in the United Kingdom not permissible by the Human Fertilisation and Embryology Authority.

Children born after in vitro fertilisation will have a very different view of the justification for exposing them to any excess risks, especially if they realise that safety considerations were not a priority for the people who had helped their parents conceive them. What is needed here is a large prospective population based study of the birth registry, with naturally conceived children as controls to start addressing the question of risk definitively. Surely now is the time.

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