a recent report in the *Lancet* has called for an end to routine antenatal admissions for women with twin pregnancies if the pregnancy is 'uncomplicated'. This follows an Australian study which showed that mothers who were randomly allocated outpatient care from the 26th week were less likely to have high blood pressure, discomfort and premature labour, compared with mothers randomly made to stay in hospital, especially if they had other children at home. This is presumably the sort of advice which underfunded hospitals will be happy to follow.

Of course, doctors have been advising bed rest in the hope of preventing a premature delivery. This is one of the main hazards of a higher multiple birth, resulting in problems for everyone concerned. For the babies there is an increased risk of cerebral palsy, with children who weigh less than 1,500 grams (3 lb 5 oz) at birth being most at risk, (a rate of 68 per 1,000 compared with 2 per 1,000 in the general population). In fact all triplets and higher multiples are more at risk of cerebral palsy (17.4 per 1,000 children), whatever their birth weight. Low-birth-weight children are also more likely to be readmitted to hospital for other reasons.

For the parents, having three or more premature babies in special care units causes stress; and if they are split up between various hospitals as they often are, the logistics of visiting them may be impossible, especially because the mother may be far from well. Over a quarter of mothers of triplets and over a third of mothers of quads have medical problems after the birth which include haemorrhage, anaemia, infections and high blood pressure.

For hospitals working on a tight budget the number of intensive-care cots has to be kept down. In fact over the country the number has actually been reduced. And it is extremely unlikely that three will be empty in the same hospital at the time when triplets are born. The number of sets of triplets born each year has more than doubled with the emergence of private IVF clinics. Conceived profitably by private medicine, the problems of neonatal care fall on a public health service that is short of money. The report estimates that at 1988 prices the National Health Service cost of hospital care is £5,000 for a set of twins, £12,000 for triplets and £25,000 for quads or more.

Three, Four or More makes compelling reading with its combination of statistics and quotes from parents, the cost to whom in money, energy and emotion is enormous. But relationships between multiples are among the strongest and most enduring of any human relationships. □

John Galloway is at the Cancer Research Campaign, 2 Carlton House Terrace, London SW1Y 5AR, UK.

Ten years on

B. Hogan

Transgenic Animals: Edited by N. L. First and F. P. Heseltine. *Butterworth-Heineman: 1991. Pp. 358. £60, $75.*

A DECADE has now passed since the first transgenic mice were generated by the microinjection of cloned DNA into the pronuclei of fertilized eggs. The production of transgenic mice is now almost a routine procedure, and microinjection has also been used to introduce foreign DNA into rats, pigs, sheep and cows. More recently, it has become clear that the targeting of mutations to specific genes by homologous recombination in murine embryonic stem (ES) cells, although technically much more difficult than microinjection, also has the potential to become a standard experimental tool. At a time when many scientists are dreaming of future possibilities opened up by the intrepid pioneers of ES cell manipulation, it is useful to step back a little and reflect on what has been achieved during the decade of research with transgenic animals. What hopes have been fulfilled and what unexpected insights gained? Equally important, what problems remain unsolved and what has proved to be more difficult than expected? How will ES cell technology answer questions that cannot be addressed using microinjection? A review volume, covering these and other topics would be very useful, and *Transgenic Animals* goes some way towards providing a broad overview for people in medical and agricultural research interested in learning just what transgenic technology has to offer them.

Unfortunately, though, the contributions to this book are rather uneven and the potential reader must be prepared to pick and choose from a mixed offering. The problem arises from the fact that *Transgenic Animals* is the proceedings of a workshop convened in Bethesda in 1988 by the National Institute of Child Health and Human Development. The staff of NICHD have been staunch supporters of research using transgenic and ES cell technology, and the goal of the meeting was to bring the achievements and potential benefits of transgenic research to the attention of a wide audience, and to place the research within the context of other work on gene regulation, gene therapy and models of human disease. Inevitably, some of the speakers presented only current research results which are now rather dated. It would have been better if these papers could have been omitted in favour of expanding others in which experimental data are presented clearly within the context of general principles.

One of the major achievements of transgenic technology has been the ability to define DNA sequences controlling complex temporal and tissue-specific patterns of gene expression. In many cases, the delineation of positive and negative regulatory elements would have been impossible without transgenic technology. Perhaps the most celebrated example is the discovery of the locus control region (LCR) far upstream of the human β-globin gene cluster. This LCR is required for high levels of expression of the different β-globin genes in a developmentally correct sequence, and is thought to influence the structure and accessibility of chromatin over a considerable distance. Other examples of tissue-specific gene expression are reported in this volume, including studies with genes for alphafetoprotein, histocompatability antigens, and milk and muscle proteins, thus adequately covering a range of regulatory strategies.

Another theme of *Transgenic Animals* is the application of transgenic technology to the production of models for human disease. The goal has been to generate animals which can provide real insight into complex disease processes and act as a test bed for therapeutic intervention, rather than just pathetic examples of pathology and deformity. In some cases success has been achieved, for example in producing models for multistage progression in cancer or for testing vaccines. In other cases mouse models have been disappointing, either because they have produced no real insight or because the disease phenotype was not obtained. For example, homozygous $HPRT^-$ mice show none of the symptoms of Lesch-Nyhan disease because of a fundamental difference in purine metabolism between mice and humans. Overcoming such problems requires the ability to introduce genes into a range of experimental animals, a topic well covered in this book. The recent observation by R. E. Hammer and colleagues that transgenic rats carrying the human HLA-B27 gene display the symptoms of the complex inflammatory disease ankylosing spondylitis, whereas transgenic mice do not, testifies dramatically to the importance of a multi-organism approach. The pluses and minuses of introducing transgenes into farm animals for agricultural improvement are also adequately addressed, and the book concludes with a chapter on the ethics of patenting transgenic animals. In summary, this is not a 'how to' book. Nor does it provide a comprehensive account of all achievements using transgenic animals. Rather the articles are a reflection of research projects as they really are; some good, some indifferent, and some so good they make it all worthwhile. □

B. Hogan is in the Department of Cell Biology, Vanderbilt School of Medicine, Nashville, Tennessee 37232, USA.