intravenous method is preferred, preferably selectively to reduce workload and cost. Patients at low risk from surgery who have ductal stones are probably best managed by an open operation, while endoscopic clearance of the duct may be reserved for those at greater risk from surgery and those whose stones are identified after laparoscopic cholecystectomy.

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Tomorrow's biotechnology

Beyond the ploughman's lunch

Doctors who are so overworked that they have to browse through their *BMJ* while indulging in that uniquely British dyspeptic experience the ploughman's lunch can at least take consolation in the knowledge that they are partaking in the first success story of biotechnology. For, as pointed out in the introduction to the National Economic Development Council's recent publication on the future of biotechnology,¹ this exciting field has evolved through three stages: the "old" or traditional biotechnology, covering such activities as beer and cheese making; the "middle period," starting in the mid-1940s, when fungi and bacteria were used to produce antibiotics and food and animal feed; and the "new" age, beginning in 1973, which encompasses genetic engineering and modern cell biology.

This lively report leaves its readers in no doubt that even if the biotechnology industry does not change their lives too much it will certainly have a major impact on those of their children. A glance at its index highlights the enormous scope of this new field, ranging from health care through agriculture and the food and chemical industries to the environment and bioelectronics. There is much here to interest doctors and to strike terror into the hearts of those who manage our health services.

According to the chief executive of Genentech, a leading biotechnology company, "by the turn of the century . . . every drug will be touched in its development by biotechnology."² Because profit margins are high in the pharmaceutical industry biotechnology companies have found it relatively easy to raise development finance and have been quick to apply the new techniques of recombinant DNA to the production of therapeutic proteins. Considering the complex-

ity of the technology, the industry has moved remarkably fast. The council's report lists over 35 new products that are being subjected to clinical trial. Sales figures for biotechnological pharmaceutical products in 1990 show that growth hormone and erythropoietin have already broken the £300 million turnover barrier and that interferon alfa, human insulin, tissue plasminogen activator, and hepatitis B vaccine look like catching up before long.

No doubt exists that industry will continue to exploit the enormous possibilities of this new technology. Indeed, the basic scientists already seem to be moving too fast for the doctors. Over the past five years a bewildering battery of growth factors, hormones, and other biological mediators have been isolated; in many cases they are still waiting for the right disease to treat.

Something else that should benefit enormously is the control of infectious disease. Biotechnology together with an improved understanding of the immune system offers the opportunity to develop safer and more effective replacements for existing vaccines as well as new ones for previously unpreventable diseases. Recent innovations include subunit vaccines, anti-idiotypic technology, and the application of genetic engineering to produce peptides or glycoproteins.

As well as the production of therapeutic proteins and vaccines biotechnology offers many other possibilities for medical care, some not quite so obvious. The dream of safe alternatives to blood has recently come a step nearer to reality with the production of human haemoglobin in yeast. Vascular implants are being made more compatible by treatment with growth factors, and graft rejection is being tackled by the use of specific antibodies bound to magnetite to permit magnetic

removal of T cells. Monoclonal antibody technology and the humanising of rat monoclonals by genetic engineering offer many possibilities; over 50 different drugs based on monoclonal antibodies are under development for treatment of cancer, particularly colorectal and ovarian cancers. Similar products are being developed for the treatment of hepatitis and various refractory viral infections and even for attacking blood clots. Human gene treatment, so long a dream, now seems to be a genuine possibility. One form of combined immunodeficiency disease, due to adenosine deaminase deficiency, has been successfully treated by inserting the missing gene into patients' lymphocytes and reinfusing them.

Another promising therapeutic lead has developed from "antisense" technology, which is more promising than its name suggests. When genes are transcribed it is from one of the complementary strands of DNA, called the "sense" strand. The resulting messenger RNA is a mirror image of this strand. If an appropriate antisense sequence can be introduced into a cell it will bind to the messenger RNA and, in effect, inactivate the particular gene. So far the major tour de force of this technology has been the production of tomatoes with a longer shelf life. Though it is not envisaged that we increase our geriatric problems by prolonging our own shelf lives, this new approach holds out exciting possibilities for the treatment of cancer and viral disease. For example, by using short lengths of antisense DNA to shut off key genes in the development of malignant transformation it is hoped to control certain tumours.

The biotechnology industry has already developed over 400 clinical diagnostic systems, many of which are already in clinical use. They are based on a wide variety of new techniques, including monoclonal antibody, DNA probes, and the enzyme linked immunosorbent assay (ELISA), and have uses in almost every branch of diagnostic pathology.

Of course the new biotechnology era is not without its problems. The new report reviews the many monitoring and regulatory bodies that are springing up, both nationally and in the European Community. Collectors of acronyms are having a heyday; already the United Kingdom has spawned the Genetic Manipulation Advisory Group (GMAG), the Advisory Committee on Genetic Manipulation (ACGM), and now the Advisory Committee on Releases to the Environment (ACRE) to control new and potentially dangerous laboratory procedures, containment, the development of transgenic animals, and the release of genetically engineered micro-

organisms into the environment, and so on. There are still ethical concerns about patenting human DNA and human genetic engineering. The guidelines to regulate human gene therapy, which have been drawn up recently by the Clothier committee, will be published soon and should do much to reassure the public that this new departure does not open up any fundamentally new ethical problems.

Clearly, therefore, the new biotechnology is no longer an Orwellian dream but is now with us. As pointed out by the National Economic Development Council, this development has reached the point at which industry can no longer ignore it, and those companies that are not already participants must now ensure that they are fully aware of how it might affect them. Large technological change invariably leads to industrial casualties, and British companies must try to avoid being among them. No doubt our health service managers will view all this with their customary gloom. The products of biotechnology are expensive, but this is mainly because at this stage of its evolution the industry is working on a small scale. Biotechnology is no different from any other technology; the development of technological know how and the spreading of overheads over a greater volume of production will inevitably drive down unit costs.

All this is good news for British industry and for the medical world. The new biotechnology, however, will not revolutionise clinical practice overnight. In one sense the industry has tried to run before it can crawl. Perhaps it should not have been surprised to discover that one of the earliest forms of interferon to be produced by recombinant DNA technology was useful only for treating pharyngeal warts and a rare form of leukaemia. The real excitement of this field, and of molecular medicine as a whole, is that we now have the tools to tackle some of the intractable health problems of Western society. With a little patience and better collaboration between the industry and the medical profession it should be possible to exploit to the full the enormous potential of this extremely exciting new field.

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1 National Economic Development Council. *New life for industry. Biotechnology, industry and the community in the 1990s and beyond*. London: National Economic Development Office, 1991.

Restraint of children in cars

Education not just legislation

The introduction of seat belts in motor vehicles and laws to enforce their use have generally been accepted as reducing the severity of injuries sustained in motor accidents, and more and more countries are introducing legislation to improve their use. Nevertheless, seat belts themselves may cause injuries—potentially to most structures from the neck to the pelvis.¹⁻³ Now that the need for seat belts has been accepted, it is time to spare some effort to ensure that they are fitted and used properly. This applies particularly to the restraints used for small children.

Although studies have reported on the effectiveness and the complications of seat belt use by adults,^{4,5} few have examined the effectiveness of restraints in children.⁶⁻⁸ In 1989 legislation was introduced in the United Kingdom that required the

restraint of children in rear seats of cars when suitable equipment was fitted. Following the introduction of such legislation, in both the United Kingdom and elsewhere, there have been an increasing number of reports of injuries, in particular to the spine,⁹⁻¹¹ to children restrained in cars involved in road traffic accidents. Such injuries will probably become more common in the United Kingdom as child restraints are increasingly used, both correctly and on occasions incorrectly. We have recently been aware of a number of spinal injuries in children who were improperly restrained. In one particularly sad case an infant sustained a "hangman's" fracture of his upper cervical spine, and permanent tetraplegia, after improper restraint during a road traffic accident.