In cancer and in chronic viral infections prolonged treatment with interferon may be necessary. Though the supply from Cantell has been augmented by using cultures of fibroblasts and lymphoblasts, it was inadequate for the demands of research groups even before the recent intense publicity propagated the idea that interferon might be an effective anticancer agent. In the past year, however, several groups have described the successful expression in *Escherichia coli* of genes for human leucocyte (IFNα) and fibroblast (IFNβ) interferon.[2-6] Yields from bacterial fermentation may be considerably higher than the optimum yields of natural interferons from eukaryocytes. Bulk culture of bacteria is easier than that of diploid cells, and improvements in both cultivation techniques and gene expression may be expected to increase these yields considerably.

In theory, recombinant technology is simple. Interferon messenger RNA is extracted from cells stimulated to produce interferon and a complementary DNA copy made. Several short nucleotide sequences are added to ensure the correct expression of the desired protein. These include a promoter sequence (which can be controlled by the concentration of a specific substrate such as tryptophan); a ribosome-binding site; and a linker molecule, which determines the exact site for the initiation of gene translation. The gene sequence is next attached to a plasmid vector which will naturally transform an appropriate strain of bacteria. Vector plasmids also transmit a pattern of antibiotic resistance useful in identifying successful transformants.

In practice, however, the genetic codings for human interferons seem to be complex: there are at least eight distinct genes that code for different IFNα molecules.[7] Two IFNβ messenger RNAs have been identified,[8] but there is no evidence for the expression of both of these as different IFNβ proteins. On the other hand, the multiplicity of IFNα forms has recently been confirmed using a technique of amino-acid mapping of lymphoblast interferon peptides after treatment by trypsin and chymotrypsin.[9]

This multiplicity of molecular forms might possibly account for the varied functions of interferons, but the only difference apparent so far is in the cell-species selectivity of the antiviral potency of two different IFNα gene products.[10] This suggests that cell-surface receptor sites for interferons are highly specific.

Fears that the gene product would not be active in vivo have been allayed by the recent report that recombinant IFNα protects squirrel monkeys against fatal infection with encephalomyocarditis virus.[3] Another group[11] has shown that one recombinant IFNα may enhance both natural killer-cell and antibody-dependent T-cell cytotoxicity and may inhibit the growth of Burkitt lymphoma cells—activities which may be partly responsible for interferon's anticancer effect.

Contrary to earlier suggestions, pure IFNα may not be glycosylated, so that a gene product would closely resemble natural interferon. Nevertheless, natural IFNβ probably is glycosylated; since the gene product will not be, differences in activity or pharmacokinetics may emerge.

Interferons prepared from *E coli* will be contaminated with unidentified bacterial proteins, which may or may not represent more of a hazard to patients than unidentified proteins from pooled human leucocytes, from fibroblasts exposed to antimetabolites, or from lymphoblasts transformed by Epstein-Barr virus. Chemical purification of interferons has been difficult because of the small amounts of protein being handled and their tendency to lose activity. Monoclonal antibody affinity chromatography[12] should, however, provide a method for absolute purification, though a different antibody will be needed for each separate antigenic subspecies.

Only 20 months elapsed from the first report of the successful expression of the human insulin genes in *E coli*[13] to testing the product in volunteers,[14] and we may expect progress with interferon to be comparably swift. The scientific merit of this work is undeniable, and our knowledge of the biology of the interferon system will be greatly advanced as the structure and multiplicity of interferon genes are understood. Whether the present evidence of the clinical usefulness of interferon provides financial justification for investment in this technology remains to be seen. Certainly, when enough interferon is available from *E coli* for clinical use it ought firstly to be used to augment the meagre supplies of natural interferon in controlled clinical trials. In this way we can establish its value before it is distributed widely in the widespread belief that it is a panacea.

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Leucocyte scanning in abdominal surgery

Recent efforts[1] at reducing the ill effects of intraperitoneal sepsis, including residual abscess, have been successful in lowering morbidity,[2] but collections of pus still occur. Clinical circumstances, problems of origin, and the masking effects of prolonged courses of antibiotics may occasionally make diagnosis difficult. Conventional imaging with straight *x*-ray films, contrast studies, scintiscanning, and computed axial tomography all contribute to localisation; nevertheless, in a few instances the patient remains ill, and, though a septic focus is suspected, none can be found.

Acute inflammation leads to increased vascularity and the local accumulation of leucocytes, and logically an imaging technique could exploit these features for diagnosis. Two lines of approach have been tried. Radioactive gallium citrate is concentrated in vascular areas[3-7]; and this isotope[4 8] and others

such as technetium-99m,[9] chromium-51,[10] and indium-111[11] may be attached to leucocytes. All these isotopes are gamma emitters, so permitting their detection by camera or rectilinear scanner. Gallium citrate unattached to leucocytes has the disadvantage of being concentrated in any area of high vascularity such as a tumour and of being excreted by the colon. Of the leucocyte markers, indium-111 seems the most suitable.[12] The technical trick is to chelate the emitter, indium, to a molecule—hydroxyquinalone—which is lipid soluble and so penetrates the leucocyte cell membrane. Such beaconed white cells remain viable, and when reinjected join their colleagues in any inflammatory focus. Indium has the additional merit of a relatively short half life (67 hours), which allows scans to be repeated if necessary.

Recently Coleman and his colleagues[13] have reported on a series of 58 patients in whom 68 such scans were undertaken. They found that the technique had a high sensitivity—abscesses were always associated with abnormal scans—but a low specificity because of the influence of inflammation short of abscess formation, superficial wound infection, renal transplant rejection, and other causes of increased vascularity and leucocyte accumulation (such as an accessory spleen). False-negative results have been reported to reach 12% in other series.[14]

The surgeon will accept with alacrity that these results are interesting and point a possible way towards improvements in management of patients. Nevertheless, the question not answered conclusively by these studies is the proportion of patients with abscesses that could not be detected by less complicated and less expensive means. Why bother to show that a hot red wound concentrates indium-111-labelled leucocytes or that a patient with fever, pain in the shoulder tip, and a gas-liquid bubble under the diaphragm has a hot spot on a leucocyte scan? In such patients the diagnosis is already obvious. In yet others it may be made by the judicious choice of a simpler or more readily available imaging technique. So the proponents of leucocyte labelling must show that their efforts yield dividends by uncovering concealed and dangerous collections. Six of the 12 patients in one series investigated with gallium had pyrexia of undetermined origin[5]; two of the nine abscesses Coleman *et al*[13] identified with indium-111 were diagnosed only by scanning. Conclusive evidence of the utility of scanning in all but exceptional cases is not yet forthcoming. Until it is, alert clinicians prepared to study their patients diligently need not feel too deprived because they cannot have indium leucocyte studies on tap. The technique will probably find its place as one which should be available in a few centres for the referral of those few patients with a true "pyrexia of undetermined origin" after abdominal surgery.

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Prevention of haemolytic diseases of the newborn due to anti-D

In Caucasian populations and without treatment about one in 20 children born to Rh-negative mothers are affected with haemolytic disease due to anti-D sensitisation. Before treatment the mortality was probably about 20-40%, but with the introduction of exchange transfusion by Diamond[1] the prognosis for those born alive dramatically improved, and in skilled hands a survival rate of 99% has been reported.[2] The findings by Finn *et al*[3] and by Freda and Gorman[4] that the injection of anti-D immunoglobulin post partum would often prevent the maternal production of antibodies led to a rapid decline in the incidence of the disease and hence also in mortality. In 1970, anti-D immunoglobulin became generally available, and by 1976 many countries were reporting that mortality had been cut by more than half.[5]

At a meeting at McMaster University[5] in 1977 anti-D was reported to be about 90% effective in preventing Rh immunisation by pregnancy, the incidence falling to about one in 200 from the expected rate of one in 20. When immunisation does occur about one-third of the cases are due to anti-D sensitisation appearing during the first pregnancy; in another third it is due to failure to give anti-D immunoglobulin; and in the remainder it is due either to transfusion of Rh-positive blood or to failure of the injected anti-D immunoglobulin to prevent sensitisation. Sensitisation during the first pregnancy results from fetal cells crossing the placenta, usually from the 29th week of pregnancy onwards, since sensitisation is uncommon before this time. When immunoglobulin anti-D is given at 28 and 34 weeks of gestation it substantially reduces the incidence of sensitisation during the first pregnancy. General, widespread antenatal use of anti-D immunoglobulin would, however, require up to four times the amount required with the present practice of giving it only postnatally.

Hence if antenatal treatment is to be introduced, the benefits must clearly outweigh the disadvantages. To assess the benefits Tovey[6] investigated all mothers from about one-third of the population of Britain in whom anti-D sensitisation was found for the first time during 1978. In this sample there were four infant deaths but only two of these were in first-born babies to Rh-negative mothers. By extrapolation to the whole population Tovey suggested that antenatal injection of anti-D immunoglobulin would prevent about six to eight perinatal deaths from haemolytic disease each year. He also calculated