and abnormal¹⁸ (carcinomatous) cells and to the antigens of infectious agents will allow improved identification, separation, and classification of cells and provide means for diagnosis in disease states. Such antibodies tagged radioisotopically, by fluorescent dye or by the immunoperoxidase technique, could be used in vivo to localise inflammatory or neoplastic lesions.19

Monoclonal antibodies may even prove useful in some treatment regimens requiring passive immunisation. Whether or not monoclonal antibodies in isolation will have a use in treating infections remains uncertain, though encouraging results have been achieved in malaria.20 The ability to raise monoclonal autoantibodies to relatively crude antigen preparations from patients with autoimmune diseases should not only provide a means for subsequent purification and characterisation of the antigens concerned but will improve assay systems for the detection of such diseases. Possibly the establishment of antibodies to these antibodies (anti-idiotypic antibodies) may provide a selective means for controlling such diseases by manipulation of the aberrant autoimmune response.²¹ The most exciting therapeutic potential of these agents, however, is in cancer. Toxic agents such as ricin or diphtheria toxin may be coupled to monoclonal antibodies raised to specific tumour cell markers and so provide a means for the toxin selectively to home-in on the tumour and kill it.22

The potential applications for monoclonal antibodies in the purification of substances in diagnosis and treatment seem limitless. Their production, however, is not without problems, and many questions still have to be answered. These include the cost of production; technological difficulties in extraction, purification, and concentration; overspecificity; the remaining uncertainty about how immortal the hybridomas producing these antibodies really are; and, finally, the ethical questions that will need answering when the products of human hybridomas are ready for clinical use. All these problems are attracting attention as technological development progresses towards maturity, but in no way do they diminish the phenomenal importance and potential of the work of Milstein and his colleagues3 or lessen the likely rewards still to come.

A M McGregor

Wellcome Senior Research Fellow, Welsh National School of Medicine, Cardiff CF4 4XW

Technicians 1980;31:113-8.

- ¹ Burnet FM. The clonal selection theory of acquired immunity. Cambridge: Cambridge University Press, 1959.
- ² Raschke WC. Plasmacytomas, lymphomas and hybridomas: their contribution to immunology and molecular biology. Biochim Biophys Acta 1980;605:113-45.
- ³ Köhler G, Milstein C. Continuous cultures of fused cells secreting
- antibody of predefined specificity. Nature 1975;256:495-7.

 Galfrè G, Milstein C, Wright B. Rat > rat hybrid myelomas and a monoclonal anti-Fd portion of mouse IgG. Nature 1979;277:131-3.
- ⁵ Olsson L, Kaplan HS. Human-human hybridomas producing monoclonal antibodies of predefined antigenic specificity. Proc Natl Acad Sci USA 1980;77:5429-31.
- ⁶ Croce CM, Linnenbach A, Hall W, Steplewski Z, Koprowski H. Production of human hybridomas secreting antibodies to measles virus. Nature 1980;288:488-9.
- ⁷ Pontecorvo G. Production of mammalian somatic cell hybrids by means of polyethylene glycol treatment. Somatic Cell Genet 1975;1:397-400.
- ⁸ Littlefield JW. Selection of hybrids from matings of fibroblasts in vitro and their presumed recombinants. Science 1964;145:709-10.
- ⁹ Engvall E, Perlmann P. Enzyme-linked immunosorbant assay (ELISA). Quantitative assay of immunoglobulin G. Immunochemistry 1971;8: 871-4.
- ¹⁰ Köhler G, Milstein C. Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion. Eur J Immunol 1976;6:511-9. 11 Paul J. Cell and tissue culture. 5th ed. Edinburgh: Churchill-Livingstone,
- 12 Wright P. Production of monoclonal antibody ascitic fluid and sera in mice with hybrid myeloma tumours. Journal of the Institute of Animal

- ¹³ Goding JW. Use of staphylococcal protein A as an immunological reagent. J Immunol Methods 1978;20:241-53.
- 14 Awdeh ZL, Williamson AR, Askonas BA. Isoelectric focusing in polyacrylamide gel and its application to immunoglobulins. Nature 1968;
- 15 O'Farrell PH. High resolution two-dimensional electrophoresis of proteins. 7 Biol Chem 1975:250:4007-21.
- ¹⁶ Secher DS, Burke DC. A monoclonal antibody for large-scale purification of human leukocyte interferon. Nature 1980;285:446-50.
- ¹⁷ Reinherz EL, Schlossman SF. Regulation of the immune responseinducer and suppressor T-lymphocyte subsets in human beings. N Engl J Med 1980;303:370-3.
- ¹⁸ Schlom J, Wunderlich D, Teramoto YO. Generation of human monoclonal antibodies reactive with human mammary carcinoma cells. Proc Natl Acad Sci USA 1980;77:6841-5.
- 19 Levine G, Ballou B, Reiland J, Solter D, Gumerman L, Hakala T. Localization of I-131-labeled tumor—specific monoclonal antibody in the tumor bearing BALB/c mouse. J Nucl Med 1980;21:570-3.
- ²⁰ Yoshida N, Nussenzweig RS, Potocnjak P, Nussenzweig V, Aikawa M. Hybridoma produces protective antibodies directed against the sporozoite stage of malaria parasite. Science 1980;207:71-3.
- ²¹ Roitt IM, Cooke A, Male DK, et al. Idiotypic networks and their possible exploitation for manipulation of the immune response. Lancet 1981;i:
- ²² Olsnes S. Directing toxins to cancer cells. Nature 1981;290:84.

Therapeutic embolisation

The development of techniques for inserting a catheter percutaneously and manoeuvring it into almost any artery with safety and confidence is one of the major advances in medicine. At first the main aim was to obtain better angiograms, but now arterial catheterisation has acquired increasing therapeutic value. In addition to allowing regional infusions of drugs and mechanical dilatation of stenoses in arteries, catheters may now be the route by which the radiologist deliberately introduces emboli into vessels feeding tumours, vascular abnormalities, or sites of bleeding.

The principle of embolisation is not new. In 1904 Dawbarn injected paraffin and Vaseline into the arterial supply of tumours¹ and "so deprived them of blood as to permit after a short time an extirpation of the tumours not otherwise possible." The burgeoning specialty of "interventional radiology" is, however, a product of the last 15 years. The agents now introduced as emboli include autologous clot, Gelfoam, muscle, Silastic balls, silicone balloons, steel coils, and cyanoacrylic glue. Some produce permanent occlusions, some temporary. There is, however, no agreement about which agent is the best for each indication.²

Ease of access and straightforward vascular anatomy have made the kidney the most common target for the doctor practising embolisation. The vascularity of hypernephromas³ and Wilms's tumours⁴ may be reduced before surgery, and pain and haematuria from inoperable growths may be alleviated.⁵ Bleeding after biopsy or blunt trauma to the kidney may be effectively controlled, often without loss of the whole of the kidney.6 The technique has also been used to "switch off" the kidneys of hypertensive patients already having haemodialysis.7 Last week at p 1086 May reported the use of embolisation to avoid nephrectomy after ureteric trauma. Elsewhere in the urinary system embolisation has proved effective in the control of haematuria from unresectable cancer of the bladder, and it may even be a rational as well as effective treatment for priapism.9

Patients with liver tumours, both primary and secondary, have been given useful palliation with embolisation. Pereiras et al^{10} were able to relieve pain in 80% of hepatic tumours, but survival time was not altered. Allison has reported dramatic improvement after embolisation of metastatic endocrine

tumours.¹¹ Embolisation of the spleen has had a less happy history. Treatment of the whole spleen for enlargement may produce pain, abscess formation, septicaemia, and even splenic rupture; partial embolisation may be as effective a treatment with a lower morbidity.¹⁰

Gastrointestinal bleeding in patients who are not fit for surgery is a common and unsolved problem for which embolisation may offer help. Reuter has reported 40 successful embolisations to control such haemorrhage. Bleeding from gastro-oesophageal varices complicating portal hypertension has also been successfully attacked, with access to the portal circulation by a percutaneous transhepatic route. Nevertheless, the risks and effectiveness of this technically impressive manoeuvre must be weighed against the less invasive technique of injection of the varices through the oesophagoscope.

Angiomas, particularly those containing arteriovenous fistulae, provide another example of a surgical problem for which embolisation has shown benefits, either as the definitive treatment or as a preliminary manoeuvre to convert a difficult or impossible operation into a straightforward one. ¹³ Particular success has been achieved in nasal angiofibromas. ¹⁴ Among other clinical conditions for which embolisation has been tried and found helpful are epistaxes, ¹⁵ haemoptysis, ¹⁶ aneurysms, ¹⁷ postpartum haemorthage, ¹⁸ and haemorthage after pelvic fractures. ¹⁹

The technique is still in an early stage of development, yet surprisingly few complications have been reported. Symptoms due to ischaemia or infarction of the treated organ are to be expected. Strokes may result either from overflow of emboli into the cerebral circulation or from failure to predict the anatomy and haemodynamics of head and neck angiomas and arteriovenous fistulae, and are particularly distressing complications.²⁰ Nevertheless, fortunately in the hands of experts they are rare. Most other complications are due to specific problems of technique and may be expected to be less common as experience grows. However great that experience becomes, the technique will, nevertheless, remain complex and potentially dangerous. The technical pitfalls and the place of embolisation compared with alternative forms of treatment must, therefore, be very carefully defined before it becomes a skill embraced by every major radiology department. Furthermore, embolisation procedures should be regarded as akin to operations, needing full preoperative and postoperative care and close co-operation between radiologist and clinician.

A E Young

Consultant Surgeon, St Thomas's Hospital, London SE1 7EH

- Dawbarn RHM. The starvation operation for malignancy in the external carotid area. Its failures and successes. JAMA 1904;43:792-5.
- ² Kunstlinger F, Brunelle F, Chaumont P, Doyon D. Vascular occlusive agents. *AJR* 1981;**136**:151-6.
- ³ Goldstein HM, Medellin H, Beydoun MT, et al. Transcatheter embolisation of renal cell carcinoma. AJR 1975;123:557-62.
- ⁴ Danis RK, Wolverson MK, Graviss ER, O'Connor DM, Joyce PF, Craddock TV. Peroperative embolisation of Wilms' tumors. Am J Dis Child 1979;133:503-6.
- Muller JH, Engel D, Waigand J, Mebel M. Late results following palliative vascular embolisation in inoperable kidney tumours. Z Urol Nephrol 1978;71:481-93.
- ⁶ Curet P, Roche A, Riche MC, Merland JJ, Doyon D. Therapeutic embolisation for traumatic renal haemorrhage. *Nouv Presse Med* 1980; 9:2633-6.
- ⁷ Seybold P, Lux E, Grosse Verhold R, Zeitler E, Gessler V. Embolisation of renal arteries: an alternative to nephrectomy in the treatment of patients with dialysis and malignant hypertension. Klin Wochenschr 1980;58:696-700.
- 8 Carmignani G, Belgrano E, Puppo P, Cichero A, Giuliano L. Transcatheter embolisation of the hypogastric arteries in cases of bladder hemorrhage

- from advanced pelvic cancers: followup in 9 cases. \mathcal{J} *Urol* 1980;124: 196-220.
- Wafula JMC, Davies P. Treatment of spontaneous priapism by embolisation of internal pudendal artery. Br Med J 1981;282:363-4.
 Pereiras R, Schiff E, Barkin J, Hutson D. The role of interventional
- Pereiras R, Schiff E, Barkin J, Hutson D. The role of interventional radiology in diseases of the hepatobiliary system and the pancreas. Radiol Clin North Am 1979;17:555-605.
- ¹¹ Allison DJ. Therapeutic embolisation. Br J Hosp Med 1978;20:707-15.

 ¹² Reuter SR. Embolisation of gastrointestinal hemorrhage ATR 1979:133:
- ¹² Reuter SR. Embolisation of gastrointestinal hemorrhage. AJR 1979;133: 557-8.
- ¹³ Kaufman SL, Kumar AAJ, Roland J-MA, et al. Transcatheter embolisation in the management of congenital arteriovenous malformations. Radiology 1980;137:21-9.
- ¹¹ Lasjaunias P, Picard L, Manelfe C, Moret J, Doyon D. Angiofibroma of the nasopharynx. J Neuroradiol 1980;7:73-95.
- Merland JJ, Melki JP, Chiras J, Riche MC, Hadjean E. Place of embolisation in the treatment of severe epistaxis. Laryngoscope 1980;90:1694-704
- Rémy J, Arnaud A, Fardou H, Giraud R, Voisin C. Treatment of hemoptysis by embolisation of bronchial arteries. *Radiology* 1977;122: 33-7.
- ¹⁷ Leather RP, Shah D, Goldman M, Rosenberg M, Karmody AM. Non-resective treatment of abdominal aortic aneurysms. Use of acute thrombosis and axillofemoral bypass. Arch Surg 1979;114:1402-8.
- ¹⁸ Pais SO, Glickman M, Schwartz P, Pingould E, Berkkwitz R. Embolisation of pelvic arteries for control of postpartum hemorrhage. *Obstet Gynecol* 1980;55:754-8.
- ¹⁹ Ring EJ, Athanasoulis C, Waltman AC, Margolies MN, Baum S. Arteriographic management of hemorrhage following pelvic fracture. *Radiology* 1973;109:65-70.
- ²⁰ Dubois PJ, Kerber CW, Heinz ER. Interventional techniques in neuroradiology. *Radiol Clin North Am* 1979;17:515-42.

A new task for human growth hormone?

Human growth hormone is well established as the treatment for children with growth hormone deficiency. In Britain supplies of the hormone obtained from cadaveric pituitary glands have been such that all children who need it have been able to receive treatment, albeit under carefully controlled conditions. Unfortunately this state is threatened by a fall in the rate of pituitary collection—so that the introduction of biosynthetic human growth hormone, derived from recombinant DNA technology, will not come a moment too soon.

From time to time patients not considered to have growth hormone deficiency by the usual criteria have been said to benefit from treatment with human growth hormone, but the numbers have been so small as to have little effect on the demand for the hormone. Supply and demand may, however, be seriously thrown out of balance by a whole new prospect for treatment. In a recent issue of the *New England Journal of Medicine* Rudman *et al*² have argued that an unrecognised group of short children can benefit from human growth hormone, with a prevalence greatly exceeding that of true growth hormone deficiency, which is about 1 child in 5000.³ This proposal has implications for the supply of human growth hormone so profound that the findings of Rudman *et al* require very careful consideration.

Their paper is the fifth in a series published by the Emory group since 1978, originating in a search for a quick and economical method of assessing the long-term response of a patient to human growth hormone. Using the techniques as developed in patients with conventional growth hormone deficiency they continued to study a group of short children with what they called normal variant short stature, a term borrowed from the late David Smith. These they define as having the following characteristics: a current height and predicted adult height below the 3rd centile; a birthweight greater than 2.5 kg; no apparent cause for the short stature,