petuating the paternalistic system. Sadly, all this adds to the image that people with a mental handicap do not fit comfortably into the community.

The common law "principle of necessity" is the one that five law lords said this year should be stretched to controversial situations such as sterilisation, which has medical, social, and eugenic overtones in legally incompetent people.[5] The other principle is that of "acting in the best interests of the patient," which is interpreted to mean that the doctor should act in accordance with a substantial body of medical opinion or follow the established medical practice of the day. It is, however, in the controversial situation that there may not be an established, unanimous, or even a majority intervention. Anyone going to law for an absolute ruling for consent will be disappointed. The judge cannot given consent, and the responsibility can only remain with the doctor—who will, however, be prudent to gain the agreement from the court so that his anticipated controversial intervention "will not be unlawful."

These operational definitions may allow too much room for medical manoeuvre and insufficient backing for decisions made. Thankfully, the Law Commission and the Department of Health are investigating the law of consent, as such piecemeal guidance and legislation may not only incompletely protect the rights of the handicapped person but may infringe those rights if the seemingly unsupported doctor errs on the side of extreme caution.[6]

A notice summarising the correct legal position for this client group may with benefit be placed in all wards and departments of the local general hospital (J Bicknell, T R Gould, paper circulated within Wandsworth Health Authority). Adults with a mental handicap need their majority to be respected and the state of their legal competence assessed and acknowledged. It is hoped that with further clarification of the law it should be possible to maximise their autonomy, minimise paternalism, and provide all the health care that they require.

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Immunotherapy of human cancers

New approaches hold out promise

For years now attempts at treating cancers by immunotherapy have given disappointing results. These failures suggest that the mutations found in most human cancers do not change their antigenicity enough to make them suitable immunological targets. When antigenic differences are shown[1]—for example, in choriocarcinoma, hypernephroma, leukaemia, medullary breast cancer, melanoma, neuroblastoma, sarcoma, and some endocrine or chemically induced tumours, such as in the bladder and lung—they are often recognised only by non-human species. When antibodies raised in animals are used clinically the recipient patient may reject the antibodies. Furthermore, many tumour antigens are not useful targets—for example, B cell tumours secrete "smokescreens" of free idiotype, and these mop up any antibody-drug complexes aimed at the tumour. Studies in animals have shown that such treatment is most successful when the tumour has been reduced to a minimum by surgery or drugs and the smokescreen is thin.

Immunotherapy is described as active when the host's immune defences are recruited, passive when immune cells or antibodies from other donors are introduced, and adoptive when donor immune leucocytes confer messages to host cells.

The best prospect for active cancer immunotherapy is prophylaxis. A good example is immunisation against hepatitis B of the population of Singapore to prevent hepatocarcinoma. Other possibilities of this type include vaccines against the Epstein-Barr virus to counter endemic nasopharyngeal cancers and lymphomas, against papillomavirus to reduce cervical cancer, and against HIV to reduce Kaposi's sarcoma.

Adjuvants augment a pre-existing immune response, but their results have been poor—probably because most patients with cancer have immunological defects. The lesson from animal studies applies here too: adjuvant treatment is most likely to be successful in patients with minimal tumour who are no longer having cytoreductive treatment. The new generations of adjuvants, such as muramyldipeptide and its derivatives, may prove effective in these circumstances. The term immunostimulant is best reserved for substances producing an immune response that was previously undetectable. Most modifiers of the biological response do not cause any proliferation of lymphocytes, and even substances such as interleukin-2 tend simply to stimulate the patient's immune system to produce more of the same responses—which have already proved ineffective. Some preparations of thymic factors do increase the number of human lymphocytes bearing OKT6 (CD1), a marker for the "generation of diversity," by rearrangement of genes. The new clones that emerge in such responses may include some with activity against tumour antigens. If the tumour mass is too large the amount of antigen produced may delete such clones. Attempts to reduce tumour mass by cytoreductive agents may, however, eliminate dividing clones. The balance can be achieved: careful use of thymic factors in patients with minimal residual malignant melanoma or lung cancer has lowered recurrence rates appreciably and increased survival.[2]

Adoptive immunotherapy has been of limited success in animals[3] and humans.[4] In laboratory experiments with cultures of lymphoid cells, fetal calf serum (whose thymic factors can be lymphopoietic) has been shown to diversify the subsequent clones. Educating a patient's own lymphoid cells in vitro was the dream of previous pioneers such as Nadler and Moore,[5] and it has the advantage of avoiding the transfer of retrovirus. Such an approach could be improved by using long term bone marrow cultures with the lymphoid precursors under the influence of truly lymphopoietic immunostimulants. These tailor made treatments, however, would be very expensive; they could never be widely applicable to the one third of the population who will develop cancer. These should probably be reserved for children under 3—or for

patients who can pay for their treatment. As oncologists and surgeons get better at reducing the size of residual tumour (for example, to 10^9 tumour cells, as in a pea sized plasmacytoma[6] or choriocarcinoma[7]) trials of oral lymphopoietic immunostimulants would be justified.

Experience with passive immunotherapy with specific antibodies against tumour targets has shown that human polyclonal antibodies are the safest and the best.[8] This approach has, however, rarely achieved cures when dependent on the host for the final action (such as complement fixation or antibody directed cellular cytotoxicity). The cytotoxic drugs chlorambucil, daunorubicin, and cisplatin have been conjugated with IgG at doses preserving the immunoglobulin's half life while giving effective delivery of the drugs. Such conjugates are best used for tumours retaining their sensitivity to these drugs, and treatment may be given for many months with no ill effects (as much as 67 mg daunorubicin/kg body weight).[8] In one study of children with neuroblastomas that had been reduced in size by other treatment, cultured tumour cells were used to immunise their fathers and prepare human polyclonal conjugates. Three children with advanced disease given the conjugates had complete healing of their bony metastases and were well seven to eight years later.[8] These treatments can really be justified only in children, but in the future human hybridomas might be useful in treating other tumours showing good cross reactions (such as four fifths of neuroblastomas). Anti-idiotype responses against B cell tumours do not really qualify, and only one of 11 anti-idiotypic rodent monoclonals gave good long term results.[9] The results of using mixed hybridomas, such as Campath-1H,[10] are eagerly awaited.

New ways have been found of generating a local toxic environment when conjugated antibodies are delivered.[11] Nevertheless, using rodent monoclonal antibodies increases the risk of human hapten cross reaction, so these must be carefully screened. In general, however, single monoclonal antibodies, like single cytotoxic conjugates, are ineffective. Using a panel of humanised monoclonal antibodies from which to select a cocktail based on the immunohistochemistry of a biopsy specimen of the cancer might be more successful. Similarly, the best conjugates might be selected from in vitro culture studies of the same cancer. Such "tailoring" may again be too expensive for widespread use. When a xenogeneic product is used the host's responses to it can be removed by giving cyclophosphamide 20 mg/kg exactly 24 and 48 hours after the first exposure.[12]

Intravenous infusions of immune lymphocytes harvested from human volunteers and pigs have specific antitumour effects.[13] Such mechanisms account best for the greater success of bone marrow transplants for leukaemia in matched siblings as compared with identical twins.[14] Producing in vitro T cell clones is being explored, but using such allogeneic cells in vivo may be complicated by graft versus host disease and viral transmission.

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Risks of donor insemination

Guidelines on control of infections need further publicity

The risk of transmission of pathogens to recipients of donor insemination was highlighted by Stewart *et al* in 1985, when they documented the transmission of HIV to four out of eight recipients of cryopreserved semen from a donor without symptoms.[1] This account stimulated several reviews of mainly anecdotal reports of the transmission of genital pathogens including ureaplasma, HIV, and neisseria to recipients of donor semen.[2,3] Two more recent reports of transmission of cytomegalovirus and herpes simplex virus type 2 have again highlighted the risks of donor insemination and the problem of screening semen donors.[4,5]

Hammitt *et al* showed that cytomegalovirus could be recovered from the semen of one of four donors seropositive for cytomegalovirus even after the semen had been frozen (−196°C) for up to nine months.[4] This finding has two important implications: it has confirmed that freezing does not inactivate herpes simplex virus[6] (and HIV and chlamydia can also survive freezing[1,7]), and it has provided further support for the belief that all semen donors should be seronegative for cytomegalovirus.[8] This viewpoint is, however, contentious: such a commitment would effectively reduce the donor pool by 40%.[9,10]

At present three quarters of donor insemination clinics in Britain do not even perform serological tests for cytomegalovirus.[11] Clearly a policy for dealing with cytomegalovirus needs to be formulated, but we first need to know, for example, what the risk of infection is in couples in whom the man is seropositive but the woman is seronegative. In such cases can the use of donors seropositive for cytomegalovirus be justified?[9] What is the incidence of reactivation of the virus? Are the various strains of equal pathogenicity and equally resistant to freezing? Do men who are seropositive secrete the virus in their semen only intermittently, as the data of Hammitt *et al* would suggest?[4]

The transmission of herpes simplex virus type 2 has been proved by finding identical restriction enzyme patterns in a recipient of the donor semen and the donor.[5] The virus was transmitted to only one of the two recipients of fresh semen from a donor who was without symptoms.[5] This report raises two issues. Firstly, only one of the recipients contracted an