AIDS or specimens taken from them. "Could I catch AIDS?" is a question that will be asked with increasing frequency in Britain, and doctors need to be informed so that they can offer sensible advice not only to possible patients and their relatives but also to anyone else who may have become needlessly alarmed.

AIDS is attributed to an infection with human T cell lymphotropic virus type III (HTLV-III), and this virus has been isolated repeatedly from the blood, semen, and saliva of affected individuals. It has also been isolated from asymptomatic homosexuals and haemophiliacs. AIDS with its associated opportunistic infections or Kaposi's sarcoma or both is only one end of a range of clinical conditions caused by HTLV-III which includes persistent generalised lymphadenopathy and various combinations of fatigue, weight loss, fever, diarrhoea, and oral candidiasis. Infection results in the full blown syndrome of AIDS in only a minority of cases, but it is not known whether asymptomatic carriers of the virus are any more or less infectious than those with overt disease. Nor is it certain how many carriers go on to develop AIDS, or an AIDS related disease, because there seems to be a time lapse of up to five years between documented infection and the onset of symptoms.

The diagnosis of AIDS and its related conditions is essentially a clinical one backed up by the finding of immunological abnormalities. There is no one pathognomonic test. Further confirmation may be obtained by testing for antibodies to HTLV-III—but as yet tests for these "marker" antibodies can be carried out only in very few centres in Britain, and the results may take three to four weeks to come through. Commercial testing kits should shortly become widely available, though some are thought to give false positive results. American studies of the prevalence of antibody to HTLV-III suggest that 85-100% (depending on the assay) of patients with AIDS or progressive lymphadenopathy and of homosexuals with symptoms are seropositive. In a recent British study anti-HTLV-III was detected in 17% of homosexuals at risk and 34% of haemophiliacs, but the risk of haemophiliacs going on to develop AIDS, or an AIDS related condition, appears to be much less than that of homosexuals. (An excellent practical guide entitled *AIDS and the Blood* has recently been published and, although primarily for haemophiliacs, gives helpful advice to all those concerned with the donation and transfusion of blood.¹) Tests in unselected blood donors gave negative results, but HTLV-III antibody was found in 42% of the contacts of patients with AIDS or progressive lymphadenopathy.²

AIDS is transmitted by close contact (usually sexual) and through parenteral transmission by infected blood and plasma products. Recently seroconversion has been documented after transmission of the virus by accidental self inoculation of blood,³ but absorption of putative infected material through broken skin or mucous membranes is a theoretical rather than a proved risk.

The DHSS recently published guidelines for good practice for hospital and laboratory staff in direct contact with patients with AIDS or specimens from them.⁴ The guidelines were drawn up by the Advisory Committee on Dangerous Pathogens, and, though their "interim" nature has been emphasised, their implications have caused a great deal of concern in many service departments. For if the recommendations are to be interpreted strictly (and pressure from hospital staff may ensure that they are) each department that handles or is expected to handle suspected AIDS specimens could be expected to provide a separate room with special

equipment that is "dedicated" for the purpose. The more extensive experience in the United States suggests that such precautions are unnecessary, and common sense dictates that Britain would do well to follow that example.

In essence the American policy entails following the procedures that are already established for dealing with specimens from known or suspected cases of hepatitis B. This means a tightening of standard procedures to ensure that spillage and "splash" from machines are kept to a minimum, surfaces are kept clean, and staff report accidents promptly. Cuts or abrasions must be covered appropriately. Ideally patients suspected of having AIDS should be managed in a ward or special cubicle where the nursing staff and other hospital workers are familiar with the handling and disposal of potentially infected specimens. The DHSS guidelines suggest that suspected AIDS specimens should be flagged in a way that differentiates them from other "infectious" specimens. Whether this will serve any purpose other than to fuel the anxiety of those who are already reluctant to handle these specimens is questionable. Routine safety precautions should be adequate—a view backed up by a recent study in which HTLV-III antibody was found in none of 85 hospital employees with nosocomial exposure to specimens from patients with AIDS.⁵

The fact that tens of thousands of hospital workers in America—and probably several thousand in Britain—have been exposed to the virus and yet none has developed AIDS is reassuring for it suggests that it is appreciably less infectious than hepatitis B. There are, therefore, no grounds to suggest that transmission occurs via the aerosol route or via casual contact—or, to put it simply, by sharing a bus or a waiting room or by talking to or shaking hands with a patient with AIDS. Doctors have a responsibility to put the record straight and help people view the disease in perspective; patients with AIDS not only need our professional help but also our sympathy and understanding.

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Lectins

In 1888 at the University of Dorpat, Estonia (now in the USSR), Stillmark was studying the toxicity of castor oil seeds (*Ricinus communis*), but, finding his conscience troubled by the suffering of the animals in his experiments, he chose to work in vitro. Mixing an extract of *R. communis* seeds with blood, he made the startling observation that the erythrocytes were agglutinated and the plasma coagulated.¹ Thus began a train of research that culminated in the assassination on a London street of Georgi Markov in 1978,² and on its way cast powerful side illumination on to diverse topics such as immunology, botany, oncology, ecology, microbiology, genetics, biochemistry, allergy, and nutrition.

The haemagglutinin of *R. communis* is just one of a huge group of plant agglutinins also known as phytohaemagglutinins. This term is ambiguous, however, for it also describes

in particular the agglutinins of the common kidney bean *Phaseolus vulgaris*. The abbreviation PHA is used only for the special meaning. Since some plant agglutinins are blood group specific (and are regularly used in blood group serology³), Boyd and Shapleigh proposed the generic term "lectin" (from the Latin verb to choose).⁴ This timely and euphonious word has now been adopted to describe the whole group of molecules, whether or not blood group specific, and whether derived from plants, animals, or microbes.

In 1935 Sumner and Howell purified the lectin of the jackbean *Canavalia ensiformis* and named it concanavalin A (con A). A few months later they announced their key discoveries that concanavalin A precipitates glycogen and mucoproteins in a manner analogous to antigen-antibody precipitation, that it agglutinates granules of starch, and that this agglutination is inhibitable by cane sugar.⁵ Soon it became clear that (with a few controversial exceptions) lectins agglutinate cells and precipitate macromolecules by binding on to and cross linking their surface carbohydrates—the ubiquitous glycoproteins and other glycoconjugates. Lectins may now be defined as molecules of non-immune origin that bind to specific carbohydrate receptors with high affinity (in the same range as the affinities of antibodies, and sometimes higher). There is still hot biochemical controversy whether non-agglutinating (monovalent) molecules of this type should be admitted to the lectin club lest this cause confusion with enzymes. In their behaviour in laboratory tests lectins function very much like antibodies (though they are present *ab initio* and not produced in response to invasion), which has led plant ecologists to speculate that the lectins somehow protect the plant that makes them.

Lectinologists have co-opted the terminology of the blood transfusion laboratory to describe the "immunodominant sugar" or simply the "specificity" when talking about the specific carbohydrate receptor to which a lectin binds. This usually means the single monosaccharide which inhibits that lectin's activity at greatest molecular efficiency—for example, *N*-acetylglucosamine for wheatgerm agglutinin; α mannose and α glucose for lentil lectin, pea lectin, and con A; D galactose for the peanut lectin; and *N*-acetylgalactosamine for the lectins of soybeans and the edible snail *Helix pomatia*. None the less, the actual cell receptor that each lectin "sees" is larger than one monosaccharide: usually it contains several sugars and sometimes also amino acids. Two lectins that have the same specificity will not necessarily exert the same effects on living cells.

In 1960 Nowell added PHA to a blood sample to agglutinate the erythrocytes and thus encourage their removal, and noticed to his annoyance that the lymphocytes had also been affected.⁶ He had discovered the mitogenic effect of PHA (and many other lectins), which was the key to the current explosion of knowledge about lymphocyte physiology—and also incidentally provided geneticists with an essential tool for karyotyping. Lymphocytes in mitosis are almost never found in peripheral blood, but they were observed frequently in the blood smears of children who had eaten the North American shrub called pokeweed.⁷ Pokeweed mitogen is one of the few lectins that stimulates B lymphocytes as well as T lymphocytes. *In vitro* it triggers the production of IgE as well as other antibody isotypes.⁸ Nor is pokeweed mitogen the only lectin pertinent to IgE; both PHA⁹ and con A¹⁰ may divert an antibody response into IgE production, given the right circumstances. The discovery that grass pollens apparently share a common lectin perhaps offers a clue to why pollens so often provoke allergy.¹¹

Many of the most famous lectins are derived from food-stuffs such as grains, legumes, and tubers. Over 100 common foods have been shown to carry lectins, and the list is growing.¹²⁻¹³ Do ingested lectins reach the body tissues? Almost certainly they do. To be sure, most lectins are destroyed by cooking, but some found in, for example, wheat, carrot, maize, and banana survive cooking and may even be enhanced by it.¹³⁻¹⁴ Kidney beans that have been heated for several hours in slow cookers are likely to retain enough lectin to cause gastroenteritis, especially if not presoaked before cooking.¹⁵ Outbreaks of food poisoning have been caused by uncooked kidney beans,¹⁶ though sprouted beans usually have a low lectin content.¹⁷ Having survived cooking (or evaded it by being consumed raw—Americans ingest an average of 200 mg lectin yearly from tomatoes alone¹⁸) many lectins are then destroyed by digestion. But enough remained after an oral dose of con A¹⁹ or part cooked phytohaemagglutinins²⁰ to cause enteric signs and symptoms in man and animals, and about 2% of an ingested dose of wheatgerm agglutinin reached the faeces intact.²¹

Having survived at least partially the assaults of cooking and digestion, can ingested lectins cause disease? We do not know for sure, but many lectins are powerfully poisonous or inflammatory or both. They are particularly suited to evoke autoimmune responses, since they can bind for very long periods of time to tissues with a slow turnover, altering their antigenic composition, and virtually all body cells and most enzymes are susceptible to lectin binding; once bound, many lectins directly interfere with the immune responses mounted against them, particularly with suppressor T lymphocytes.²² Lectins have been used to produce animal models of chronic rheumatoid arthritis,²² extrinsic allergic alveolitis,²³ malabsorption of vitamin B₁₂,²⁴ and acute enteritis with cachexia.²⁵ Gluten lectins are thought, though not yet proved, to be implicated in coeliac disease.²⁶⁻²⁸ One patient with soya "allergy" was reported by Donovan and Torres-Pinedo who responded to oral administration of lactose or galactose (the specific sugars for soybean agglutinin) but not to administration of glucose or sucrose.²⁹ But the idea is too new to have been seriously evaluated by science; lectins are still "causes in search of diseases."

The potential actions of food lectins are not all bad. They might, indeed, be beneficial in, for example, the management of diabetes mellitus, since apart from slowing absorption of carbohydrates some food lectins have direct insulinomimetic and insulin sparing properties.³⁰⁻³² The science of applied lectinology is just beginning.

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A Bill that should be stopped

Last week the House of Commons gave a second reading to Mr Enoch Powell's Unborn Children (Protection) Bill. If this were to become law it would have sweeping effects. In particular, it would go against the recommendations of the Warnock report and prevent a human embryo from being created, kept, or used for any purpose other than enabling a child to be borne by a particular woman. The result would be to stop much of the research into infertility and serious genetic disorders, as well as to threaten the therapeutic in vitro fertilisation programme in Britain. The decision will also distress the thousands of couples who are hoping that future research findings might find new treatments for infertility and for the control of genetic disorders. Far too little time has elapsed since the publication of the Warnock report for calm and informed widespread debate to have

taken place; the government should not be rushed into allowing premature legislation because of the clamourings of some unrepresentative pressure groups.

A majority of the Warnock committee recommended that research might be allowed on any embryo up to the 14th day (when the primitive streak is formed), the limit recommended by the BMA.¹ Discussing the arguments about the use of human embryos, it stated that though the human embryo is entitled to some added measure of respect beyond that accorded to other animal subjects, such respect cannot be absolute and it must be weighed against the benefits of research—a view supported by the eminent theologian Professor G R Dunstan.² The public interest would be safeguarded and widespread anxiety allayed by stringent monitoring and controls—including a statutory licensing body (with a lay chairman and substantial lay representation), informed consent by the couple for the use of "spare" embryos in research, and the prohibition of transferring to a woman any embryo that had been used for research. Most of these recommendations will be introduced by the Medical Research Council in a code of practice designed as an interim measure, which emphasises the important role of additional approval by local ethics committees for individual projects.³ In some diseases research on animal models is impossible and to stop all research on embryos would be to deprive future generations of the likely benefits, in the understanding and treatment of human infertility, the detection and prevention of congenital and hereditary disorders, the reduction of spontaneous abortion, and improved contraception. It is also likely that the therapeutic in vitro fertilisation programme would largely stop, given the inevitable overlap between pure and applied research—at least in Britain, for undoubtedly such research would move to countries where it was permitted and encouraged.

Public anxiety on these issues is understandable, and it is up to doctors and philosophers to allay their fears and show the advantages of the techniques. In many ways the current alarmist statements are analogous to those made years ago about AID (artificial insemination by donor), "human guinea pigs" (experiments in man), and recombinant DNA technology. In each case full debate and explanation without premature and ill considered action allowed the public to understand the issues at stake and, with various provisos, to sanction their practice. This is what should happen in the present case: the government should come off the fence and oppose the Powell Bill on the grounds that its own considered legislation is on the way. It should stick to its plan of introducing legislation in the latter part of this year after a prolonged, informed, and calm debate has taken place.

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