weight is attached to such value judgments as distinct from more readily ascertainable gains.

Not only are clinicians uncertain about the meanings of these various terms but they often suspect that they are cloaks for cuts in services or savings in expenditure. Their shield against these threatening intruders is another much misunderstood word—ethics. They suppose that invoking ethics will ensure that clinical freedom remains sacrosanct, which in turn appears to empower clinicians to act as patients' advocates. Hence they seek to ensure that *their* patients have access to all possible services, regardless of need or expectation of benefit relative to the patients of other specialists.

In this competition for resources each bidder claims ethical justification, rather as soldiers on both sides in battle each assert that God is on their side. To deal more rationally with such difficult decision making economic appraisal is beginning to emerge. This seeks to improve the efficiency of decision making about allocating resources in the public sector by considering the rate of investment in various competing technologies that will best serve the interests of the community. A serious restraint on good decision making in the health services is the lack of good information. Economic appraisal provides techniques for systematically identifying, organising, and presenting the information required for a decision to be made. It seeks to ensure that all factors relevant to a given decision are taken into account, having been measured and valued. Given that it offers techniques not only for examining alternatives but also for generating options, economic appraisal can be creative, coming up with radical solutions that might not have occurred to the committed professionals. Such an approach acknowledges that it is not enough to show efficacy under trial conditions or even effectiveness in a wider context before diverting resources to a particular technology: it is also necessary to decide that society would best be served by not deploying a similar quantum of resources in other ways in the same or another specialty.

Although this may sound a sensible approach its adoption has been slow and patchy. Nevertheless, the Department of Health now requires economic appraisal for all major capital schemes, and Mooney and Ludbrook (p 1817), from Aberdeen, hope that this will stimulate economic appraisal of many other decisions within the NHS. A small workshop organised by these workers considered why clinicians were so reluctant to accept economic appraisal, apart from the profession's traditional conservatism and isolationism.[1] Many were probably unaware of its existence; others misconstrued its nature and purpose or dubbed it as the management fashion of the year; and yet others held that it was no more than giving fancy labels to what was already being done. Hence managers and clinicians need education and instruction, for they will have to carry out most of the appraisal, given the dearth of health economists.

In 1982 an unusual international symposium in Switzerland sought to confront the intellectual issues associated with evaluation in medicine and to break down the communication barriers that are inevitable when clinicians, policy analysts, and economists try to discuss the same problem.[2] This was no rehearsal of theoretical positions, because the symposium dealt empirically and pragmatically with three specific technologies—end stage renal disease, cimetidine treatment for duodenal ulcer, and computed tomography of the head. These interesting and unusual papers discussed the concept of "worthwhileness" and how it can be measured, and the resulting book is a classic text on economic appraisal expressed in language entirely accessible to clinicians.

The main British contribution was from Professor Alan Williams of York, who has dealt explicitly with the supposed conflict between the ethical and the economic approach to health care technologies.[3] Like those concerned with clinical trials whose ethics are sometimes challenged he turns defence into attack: unless a technology has been shown to be effective by trials and to be justifiable by economic appraisal then it might be regarded as unethical to use it. By this standard the entrepreneurial spirit associated with the clinical freedom fighters ("I know what's best for my patients regardless of trials or economics") begins to sound distinctly old fashioned.

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Infection, immunity, and blood transfusion

"Or any taint of vice whose strong corruption
Inhabits our frail blood"—*Twelfth Night* III, iv, 390

The hazards of infection from blood transfusion were the subject of the annual scientific symposium of the American Red Cross in Washington this spring. The meeting was preceded by a memorial lecture dedicated to the life and work of Professor Wolf Szmuness, whose remarkable career, devoted to the study and prevention of hepatitis B infection, matched the dramatic story of his life, swinging from the depth of despair in a Siberian labour camp to the heights of scientific success and prestige in the United States.

The general trend towards unpaid voluntary blood donation and the introduction of screening tests for hepatitis B surface antigen have greatly reduced the incidence of post-transfusion hepatitis in the United States. At present its incidence ranges between 5% and 10%, and well over 90% of these infections are caused by the non-A, non-B hepatitis viruses. Although non-A, non-B infections are usually anicteric and seem to be mild, they are nevertheless characterised by a prolonged increase of transaminase activities. Most patients who are infected go on to suffer from chronic hepatitis, and some 10-20% develop cirrhosis. Despite much effort no satisfactory serological assay for non-A, non-B viruses has been developed, probably because the amount of circulating antigen is very low. Studies on chimpanzees have confirmed that this form of hepatitis is due to one or two transmissible agents; these cause characteristic proliferative changes in the cytoplasm of hepatocytes and produce reticular inclusion bodies. The pathogen seems likely to be either an RNA togavirus or a DNA hepatitis-B-like virus—or possibly an entirely new viral agent. Non-A, non-B hepatitis is not uncommon in the United States population independently of blood transfusion; the mode of transmission is not clear. Prevention depends on better knowledge of the epidemiological features of the infection—and on the development of an appropriate serological marker.

Although other infectious diseases such as syphilis, relapsing

fever, African sleeping sickness, intestinal leishmaniasis, toxoplasmosis, and babesiasis have been occasionally transmitted by blood, malaria and Chagas' disease (American trypanosomiasis) are the two important transfusion associated parasitic diseases in many tropical and subtropical countries. The total recorded number of cases of transfusion malaria is over 3000, but the true incidence is largely a matter of guesswork. Even in some European countries the statistics are unreliable. Most cases are due to the use of donors from among the immigrant population previously exposed to endemic malaria. Proper selection of donors of whole blood and greater use of serological tests, such as indirect fluorescent antibody or enzyme linked immunosorbent assay, are the best preventive methods. The incidence of induced malaria in the United States is now very low, about one case per 4 million blood transfusions.

Chagas' disease is endemic over vast stretches of the Americas, roughly from Mexico to Argentina. About 20 million people within this area are infected, and at least 20 000 cases of Chagas' disease occur every year through blood transfusion, from infected but asymptomatic donors. Prevention of this man to man transmission depends on the rejection of infected donors, using serological tests whenever practicable. In some countries—for example, Brazil—the addition of a trypanocidal 0·4% solution of crystal violet to each unit of collected blood has been adopted, but this procedure has various disadvantages. Much research on the improvement of screening methods and on the development of trypanocidal blood additives is now in progress.

Blood transmission may occur of cytomegalovirus infections to patients undergoing open heart surgery; usually it presents as heterophil negative mononucleosis. In immunodepressed patients, however, the infection may be severe and cause pneumonia, hepatitis, pericarditis, or encephalitis. Transmission is often associated with the use of cellular concentrates, especially leucocytes. Washed concentrates provide a degree of safety; more specific markers are needed for detection of blood products infected with cytomegalovirus.

About 95% of blood donors in the United States have antibodies to Epstein-Barr virus, but the transmission of infectious mononucleosis by blood is rare. It may happen, however, if the blood has been very fresh, if a seronegative donor has been incubating a primary infection with Epstein-Barr virus, if a seropositive donor has non-protective antibodies to a capsid antigen but no neutralising antibodies, or if the blood recipient has a T cell deficiency. Illnesses induced by Epstein-Barr virus may occur in immunodepressed patients but this may be prevented by irradiation of suspected blood.

As might have been expected, the problem of the acquired immune deficiency syndrome (AIDS) and the risk of transmitting its putative viral agent by blood transfusion or by blood products aroused the greatest interest of the symposium and of the large press contingent. Suspicion that AIDS is caused by a human T cell leukaemia virus (HTLV) was strengthened by the subsequent finding of seropositivity to HTLV I and HTLV II antigens among patients confirmed to have the disease and among haemophiliacs receiving plasma derivatives such as factor VIII. An association of HTLV I with the adult T cell lymphoma has been observed in several parts of the world, and in Japan where seroconversion (shown by using the HTLV membrane antigen) was seen in recipients of blood transfusion without any evidence of AIDS.[1]

The puzzle was solved by the recent discovery by Gallo and his colleagues of a new human T cell lymphotropic retrovirus (HTLV III) probably directly responsible for the acquired immune deficiency syndrome[2]; this finding confirmed the report of an isolation of a lymphadenopathy associated retrovirus by a group from the Pasteur Institute in Paris.[3] Evidence that HTLV III is the cause of AIDS is now strong, and the proof may be definite when a case of AIDS strictly associated with transfusion permits the recovery of the specific agent from the recipient.[4]

Undoubtedly AIDS may be transmitted by blood transfusion or by blood products, though this event is rare. Of the estimated 20 000 haemophiliacs in the United States, however, about 20 have developed AIDS and a larger number have lymphadenopathy and other non-specific symptoms. About half of all haemophiliacs who receive plasma derivatives show evidence of various mild immunoregulatory disturbances (skin anergy, thrombocytopenia, lymphocytopenia, reduced T4 to T8 ratio, and so on).

Attempts at preventing the transmission of AIDS by blood transfusion have concentrated on the use of direct and indirect questioning of donors and on voluntary exclusion of homosexuals (or other groups at risk) from blood donation. Various immunological and virological tests are being used (absolute lymphocyte counts, identification of T cell subsets by monoclonal antibodies, and the presence of antibodies to hepatitis B virus, cytomegalovirus, and HTLV), although their value is only relative. The identification of HTLV III as the AIDS pathogen is an important step for the detection of carriers—and perhaps for the preparation of a vaccine. But the task is formidable—there are at least 10 million homosexual men in the United States, and many people of both sexes whose life style presents risk of infection.

The present pragmatic approach to screening over 4 million blood donors in the United States to reduce the incidence of most of the infections associated with transfusion has been successful. Three methods have been used. The first eliminates suspected donors on conceptual grounds—which has led to the policy of discouraging the use of paid blood donors. The second way is the exclusion of some donors with a risk of AIDS or history of hepatitis or their restricted use (for plasma only) if there is a possibility of other infections. The third way is the extensive use of various more or less specific laboratory tests such as that for hepatitis B surface antigen or for malaria antibodies.

A stirring evocation of challenges and opportunities of modern biotechnology with rosy visions of future achievements closed this sixteenth symposium of the American Red Cross. Its proceedings should be published with commendable speed, according to the promise of the organisers.

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