

that the N.H.S. dialysis service has failed to expand fast enough to cope with all the patients who develop terminal renal failure each year. For the foreseeable future transplantation will remain the only chance of survival for patients who cannot gain access to long-term dialysis facilities and for those unsuitable for dialysis; and many of the patients on dialysis want to risk transplantation because they find the restrictions imposed by their treatment unacceptable. Patients in all three groups—1000 or more a year—need kidneys, and the better the condition of the kidneys the better the patients' chances are that their operations will be successful.

Increasing the supply of kidneys requires a change in attitude both by the public and by doctors. The adverse press comment about organ grafting generated in the late 1960s and early 1970s by unsuccessful attempts at heart transplantation seems to have had a lasting effect, and some people—including a few doctors and nurses—still regard all organ transplantation as unjustifiable experimentation. The Transplantation Society's memorandum calls for an intensive advertising campaign in the press, on radio, and on television to tell the public about transplantation, emphasizing the youth of most of the patients and the good results of treatment. Possibly, however, those who claim that the public are ahead of the medical profession on this issue are right—transplant units recognize that in every area there are some hospitals that regularly produce cadaver organs but many others that never volunteer to provide potential donors. The reasons for this medical apathy are not known for certain—approaching relatives for consent to removal of the kidneys after the patients' death can be distressing and gives the resident doctor more work, so he may easily decide to do nothing. Clear and specific teaching about the procedure is no doubt needed both for medical students and residents; but one further certain obstacle to surgeons' access to organs is the disagreement among lawyers about the current state of the law. The memorandum proposes a simple modification to the Human Tissue Act to clarify the issue: the change would give the hospital staff legal power to remove organs after death if the doctor in possession of the body, "having made such inquiry as is both reasonable and practicable in the time available," had no reason to believe that the deceased had expressed any objection nor any reason to believe that the surviving spouse or any surviving relatives would object. Another small change would make a signed "donor card" consent in writing under the terms of the Act.

More controversial is the proposal in the memorandum that in order to reduce the warm ischaemia time (the period at body temperature when the kidney is anoxic) surgeons should be able to remove kidneys from patients with certified brain death before the heart has stopped beating. This procedure is already accepted practice in the U.S.A., France, West Germany, Belgium, Denmark, and Switzerland. Patients with brain damage are now routinely treated by artificial ventilation. Neurosurgeons have agreed criteria for deciding when brain death is sufficiently certain for it to be right to switch off the ventilator. No one is suggesting any change in the criteria used to make that decision: all that the memorandum proposes is that surgeons should be allowed to remove the kidneys before ventilation is stopped rather than afterwards—the heart may go on beating for many minutes after ventilation has ceased, and during that time the condition of the kidneys deteriorates rapidly.

The code of practice suggested in the memorandum requires that before organs are removed from a body death should be certified by two doctors, one qualified at least five years, and neither of them members of a transplantation team. Again, the

decision to stop ventilation in cases of brain death should have no connexion with transplantation considerations. If any relatives present object to the removal of organs then their wishes would be respected, says the memorandum, even if the deceased patient had himself not objected. Adequate publicity given to this code should reassure the public that the dying will always be given priority over patients who need kidneys.

The Transplantation Society's memorandum presents a reasoned case clearly and unemotionally and deserves an equally considered reply by those who disagree with it. It would be quite wrong for them to argue that kidney transplantation is an expensive luxury that the near-bankrupt N.H.S. cannot afford. Successful transplantation is no more expensive—indeed probably cheaper—than long-term dialysis as a treatment for terminal failure, and there is no ethical justification for denying treatment, known to be effective, to patients with renal failure. If treatment is not to be made available for all these patients then the Department of Health should be honest enough to admit it, and allow patients, relatives, and the medical profession to develop some system of rationing.

## Malaria Vaccines on the Horizon

Twenty-five years ago it seemed the conquest of malaria was only a matter of time. Few if any technical problems remained: the cryptic phase of the parasite, hiding in the liver during the incubation period, had been revealed, drugs of remarkable potency had been developed, the phenomenon of resistance (whether of parasites to synthetic compounds or mosquitos to insecticides) was of little importance, the global malaria eradication programme promised a rapid disappearance of the disease. Some dissenting voices indicated the obstacles that lay ahead, but their views were not popular.<sup>1</sup>

Subsequent events have brought to light many unsuspected difficulties, and the recent resurgence of malaria in several countries has made it clear that the disease will be with us for a long time.<sup>2,3</sup> However, while recent work (mainly in the U.S.A.) has led to a number of new antimalarial compounds awaiting final trials in man,<sup>4</sup> the recent upsurge of immunological research has also opened up the possibilities of a malaria vaccine.<sup>5</sup>

Attempts at active immunization of animals against malaria go back to the first quarter of the century.<sup>6</sup> A new phase of these studies started in the 1960s, when Corradetti, in Italy, confirmed that rats injected with irradiated rodent plasmodia showed a degree of protective immunity.<sup>7</sup> Since then many studies have been in progress not only on monkeys but also in man.<sup>8,9</sup>

Two main lines of research have been followed. In the first the immunizing antigen is derived from attenuated sporozoites developed in the body of infective *Anopheles* mosquitos. The second method uses the erythrocytic forms of plasmodia obtained from the vertebrate host. An advanced stage of the first approach has been reached by Clyde *et al.* in the U.S.A., who reported on promising results of a trial carried out on three human volunteers exposed to multiple bites of infected *A. stephensi* in which x-rays had decreased the virulence of sporozoites of *Plasmodium falciparum*.<sup>10</sup> One of the volunteers developed high immunity to a challenging infection with the same species of malaria parasite, and this was confirmed by

serological tests.<sup>11</sup> The resistance to infection extended for several months. However, the difficulty of obtaining appropriate amounts of the sporozoite antigen has severely limited the practicability of this method.

Previous attempts at experimental vaccination of monkeys with formolized or otherwise attenuated erythrocytic forms of the simian parasite *P. knowlesi* have been only marginally successful, because the immune response thus obtained was limited to the same strain or antigenic variant of the plasmodium and even then was of relatively short duration.<sup>12</sup> A more promising result from immunizing rhesus monkeys with isolated forms of the erythrocytic stage of *P. knowlesi* was recently reported by a group of workers from Guy's Hospital Medical School.<sup>13</sup> Their preliminary studies suggested that much of the protective malaria immunity is related to that stage of development of parasites in the blood when merozoites, derived from mature and fragmenting schizonts, are released into the plasma. This could be recognized by means of the "schizont infected cell agglutination" or S.I.C.A. test developed at the National Institute for Medical Research in London.<sup>14</sup>

The Guy's Hospital research group isolated a large fraction of merozoites from an in-vitro culture of erythrocytic schizonts of *P. knowlesi*. Some 900-2000 million merozoites emulsified in Freund's adjuvant were then injected into six rhesus monkeys. The animals showed no detectable disease, but when challenged with normally infective erythrocytic forms of *P. knowlesi* showed a considerable degree of immunity in the form of very low parasitaemia or its total absence. Though this immunity was specific to *P. knowlesi* it extended over a range of antigenic variants or strains of this parasite. Clearly vaccination with merozoites induces in monkeys a broader spectrum and a higher degree of immune response than any other method attempted until now. These results are of importance as they open the way to preparing a human vaccine against *P. falciparum*, which has a range of antigenic diversity similar to that of *P. knowlesi*.

The great stumbling block is the feasibility of a continuous in-vitro culture of *P. falciparum* as a source of antigen. Difficulties that remain to be solved were well described in two recent documents.<sup>15 16</sup> In the meantime a determined attack on the problem has been launched at the University of New Mexico, in Albuquerque, U.S.A. The American investigators have announced that their attempts at large-scale in-vitro culture of *P. falciparum* in bone marrow cells or in the blood of *Aotus* monkeys may lead "within a year or so" to clinical trials in man.<sup>17</sup>

## Prisoners' Health

The annual report of the Prison Department serves as a reminder, if such be needed in these troubled times, of the state of lawlessness in Britain and of our attempts to cope with it. Medicine is increasingly regarded (quite correctly) as an integral part of the social sciences, and its practitioners should, therefore, be concerned with all aspects of crime as one symptom of social malaise.

An apparent cause for self-congratulation in the report for 1973<sup>1</sup> is that the average daily number of people in custody in December 1973 was 35 010, the lowest figure since mid-1969. Unfortunately, taken as an index of the incidence of offences against the criminal law, this statistic is illusory, for the fall is almost certainly due to the continuing trend away from custodial sentences and the impact of the parole system, introduced in 1967, whereby prisoners are allowed to serve some portion of their sentences under supervision in the community.

In spite of the reduction in the adult prison population there is still overcrowding in many establishments. It is a sad commentary, however, that the junior detention centres for the 14-16-year-olds were full throughout the year and that the pressure on these centres increases. Nevertheless in the face of general overcrowding the health of the inmates was good; no serious outbreaks of infectious disease occurred. There were several cases of hepatitis assumed to be caused by amateur tattooing, a practice which seems from general observation to be on the increase especially among young offenders and to have become the accepted badge of a particular criminal subculture.

With the noteworthy exception of medical officers the prison service is short of staff. The unfortunate result is that the introduction and development of new methods of treatment such as the decentralization of facilities for treating prisoners with a drink problem have had to be curtailed or deferred.

The problem of drug dependence in the community at large is reflected in the 1260 persons received into custody during 1973 reported as having some dependence on drugs—though the principal medical officer of Brixton prison considered this an underestimate. He stated categorically that there is an increase in the number of drug abusers admitted to Brixton and of these there is a marked increase in those who abuse barbiturates. There has been a substantial rise in those remanded in custody for psychiatric reports: from 11 953 in 1972 to 12 542 in 1973, with a rise from 1130 to 1193 in the number of hospital orders (Section 60 of the Mental Health Act 1959). The true extent of the increases can be seen only in the context of the dramatic change since 1961, the first full year after the implementation of the Mental Health Act, when the number so remanded was only 6366 and only 838 hospital orders were made.

A most disturbing, recurring complaint is the difficulty of finding beds in psychiatric hospitals for psychiatric patients on remand. One senior medical officer went further and reported: "in one or two cases where we have had disturbed psychotic inmates on remand, National Health Service reluctance to admit them to hospital has resulted in a compromise whereby the hospital agrees to take them on a hospital order but at the end of 28 days, the agreement being that in the meantime we will get them well enough to go to hospital. This is tantamount to using a prison hospital as a secure admission ward prior to transfer to an open ward."

This is not quite as paradoxical as it may seem. Conventional psychiatric hospitals, as we have so often pointed out,<sup>2-7</sup>

<sup>1</sup> Bruce-Chwatt, L. J., *British Medical Journal*, 1954, 1, 169.

<sup>2</sup> Gabaldon, A., *American Journal of Tropical Medicine and Hygiene*, 1972, 21, 634.

<sup>3</sup> Bruce-Chwatt, L. J., *British Journal of Hospital Medicine*, 1974, 12, 381.

<sup>4</sup> Schmidt, L. H., *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1973, 67, 446.

<sup>5</sup> World Health Organization, *Symposium on Malaria Research, Bulletin of the World Health Organization*, 1974, 50, 143.

<sup>6</sup> *Lancet*, 1974, 1, 1089.

<sup>7</sup> Corradetti, A., Verolini, F., and Bucci, A., *Parassitologia*, 1966, 8, 133.

<sup>8</sup> Ward, R. A., and Hayes, D. E., *Proceedings of the Helminthological Society of Washington*, 1972, 39, Suppl. 525.

<sup>9</sup> Sadun, E. H., Wellde, B. T., and Hickman, R. L., *Military Medicine*, 1969, 134, 1165.

<sup>10</sup> Clyde, D. F., Most, H., and McCarthy, V. C., *American Journal of Medical Sciences*, 1973, 266, 169.

<sup>11</sup> Clyde, D. F., et al., *American Journal of Medical Sciences*, 1973, 266, 398.

<sup>12</sup> Schenkel, R. M., Simpson, G., and Silverman, P. M., *Bulletin of the World Health Organization*, 1973, 48, 597.

<sup>13</sup> Mitchell, G. H., Butcher, G. A., and Cohen, S., *Nature*, 1974, 252, 313.

<sup>14</sup> Brown, K. N., *Nature*, 1971, 230, 163.

<sup>15</sup> Bertagna, P., et al., *Bulletin of the World Health Organization*, 1972, 47, 357.

<sup>16</sup> U.S. Army Medical Research and Development Command, European Research Office, *Basic Research on Malaria*, 1974. Technical Report, DA-ERO-591-73-G0032.

<sup>17</sup> *Medical Tribune*, 1974, 7, 4.