rises, while that of potassium falls. Both acetazolamide and spironolactone are said to be of prophylactic value against mountain sickness, though the mechanism of their action is unknown, and that of spironolactone must be mediated by a mechanism unrelated to aldosterone antagonism. Whether the use of these drugs lessens proteinuria at altitude remains to be studied. Pines found haematuria (as detected by Bili-Labstix) in some of his subjects, which is further suggestive evidence of direct renal damage at altitude.

Acute hypoxia seems, then, in some way to lead to loss of protein in the urine. With acclimatisation this loss lessens but does not disappear. Apparently chronic hypoxia, whether due to residence at high altitude or to a right-to-left intracardiac shunt, has the same effect. Since, however, the extent of the proteinuria so caused is small and neither causes hypoproteinaemia nor otherwise threatens health, there can be no justification for taking renal biopsy samples from volunteers in high-altitude laboratories—and the morphological appearances of the kidney exposed to rapid ascent to high altitude may therefore remain unknown. There is no reason to believe that the kidney is the prime cause of the various manifestations of mountain sickness; probably the sequence of events set in train by progressive hypoxia and hyperventilation affects the kidney along with other organs.

[1] Singh, I, *et al*, *New England Journal of Medicine*, 1969, **280**, 175.
[2] Pines, A, *British Journal of Diseases of the Chest*, 1978, **72**, 196.
[3] Rennie, I D B, and Joseph, B, *Lancet*, 1970, **1**, 1247.
[4] Rennie, I D B, *et al*, *Journal of Applied Physiology*, 1971, **31**, 257.

Cancer after cardiac transplantation

The striking increase in the incidence of lymphoid neoplasms in patients who have transplants is intriguing but unexplained. Recent reports[1 2] from workers at Stanford have left no doubt that the increased risk is not restricted to renal transplantation and that there is a similar raised incidence of these neoplasms in patients who have had cardiac transplants. The first report by Krikorian and his colleagues[1] gave details on all 124 patients who underwent cardiac transplantation at the Stanford University Medical Center between January 1968 and April 1977. The median survival of these patients was 18 months, and, of the 35 deaths which occurred over three months after transplantation, four were due to malignant disease: two lymphomas, one acute myeloid leukaemia, and one adenocarcinoma of the colon. In addition, there was another case of lymphoma and two cases of squamous carcinoma of the skin among the survivors at the end of the study period. These seven cases contrast with an expected number of 0·4 in a normal population. No differences were detected in the frequency of rejection episodes or in the HLA compatibility of the graft in patients with lymphomas when compared with other patients.

A later report from the same centre by Anderson *et al*[2] gave information on an additional 19 patients, bringing the total studied to 143, and extended the follow-up to June 1978, by which time no fewer than six patients had developed lymphoma. This second report discussed several risk factors that had been undetected in the earlier study. In particular, the risk of lymphoma among recipients of cardiac transplants was found to be higher than after renal transplantation. This difference was entirely due to the very high risk of lymphomas in patients whose primary disease had been cardiomyopathy. The other risk factor was young age at transplantation. In fact, all six patients with lymphoma had had cardiomyopathy and were aged less than 40 years.

Several hypotheses have been put forward to account for the excess of lymphoid neoplasia in patients who have had transplants, and these have recently been well reviewed by Hoover.[3] They included impaired "immunosurveillance," chronic uraemia (itself immunosuppressive), the chemical carcinogenicity of immunosuppressive drugs, oncogenic viruses, chronic antigenic stimulation, and graft-versus-host reactions—or a combination of some of these factors. The fact that by no means all types of malignancy are increased in incidence argues against a simple interpretation of the concept of impaired immunosurveillance, while the unusually short induction period of these neoplasms makes the chemical carcinogenicity of the drugs unlikely. The authors of these recent reports have postulated that, as idiopathic cardiomyopathy is characterised by a defect in mitogen-induced mononuclear-cell suppressor activity, the cause of lymphomas in patients who have had transplants may be defective regulation in the immune system in the presence of the antigenic stimulation of the graft. Nevertheless, the fact that recipients of renal transplants who have polycystic disease share in the increased risk of lymphomas[3] suggests that an underlying immunological defect is not crucial for the development of these neoplasms.

Further light would be thrown on this question by information on the incidence of lymphomas in idiopathic cardiomyopathy in the absence of transplantation. We also need information on the incidence of malignant disease in patients who have not had transplants but have received immunosuppressive drugs.

[1] Krikorian, J G, *et al*, *Journal of the American Medical Association*, 1978, **240**, 639.
[2] Anderson, J L, *et al*, *Lancet*, 1978, **2**, 1174.
[3] Hoover, R, in *Origins of Human Cancer, Book A*, eds H H Hiatt, J D Watson, and J A Winsten, p 369. New York, Cold Spring Harbor, 1977.

General practice evolution

Britain is fortunate in having a competent and comprehensive general practice service. Despite the occasional well-publicised lapses in standards, most of the public are satisfied with their family doctors. But GPs are worried about the standards of service they can offer and the diminishing rewards for looking after patients. Even so, as the costs of hospital medicine rise, its staffing difficulties multiply, and waiting lists lengthen, the value to the community of a sound primary care service increases. By now, most people realise that resources for health will always be limited. Thus it is sensible to treat as many patients as possible outside the expensive institutions, provided that this can be done safely and effectively. Such a policy is economical, is usually more convenient for patients, and ensures that those who really need a hospital bed for investigation or treatment can have it promptly. A call for such a switch in work and resources from hospitals to general practice is the foundation on which the General Medical Services Committee's New Charter Working Group has built its report, published on 16 February (p 564).

The working group, chaired by Dr J G Ball, adopted a responsible approach to the task of fulfilling the Newcastle upon Tyne motion approved by the 1977 LMC Conference: "This conference deplores the reduction in general practitioners'

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