

There have been many other reports of renal transplants. However, so few control studies are available that there seems to be a need for great caution in assessing the results of any treatment. Thus with no additional treatment a transplant between unrelated persons has functioned more than five months. With transplants between closely related persons assessment is even more difficult. There have been some notable successes, but also many failures. Knowledge is rapidly increasing of the basic biology of tissue transplantation, but at present clinical transplantation must be regarded as an operation to be done only in carefully selected patients. The fact that the grafted kidney is usually taken from a living person magnifies the difficulties. For, though the donor volunteers, the responsibility for removing one of his kidneys rests with the clinician, and it is one that weighs heavily on him. Consequently, despite the many problems in taking kidneys from cadavers for grafting, it would seem reasonable to study the possibilities of using them more fully.

### CALCIUM REQUIREMENTS

The improvement of nutrition throughout the world is the main object of the Food and Agriculture Organization of the United Nations, and is also prominent in the activities of the World Health Organization. Success in this direction, however, can be measured only when accurate information is available about the requirements for various nutrients of all the different populations living and working, under widely diverse conditions, throughout the world. Committees convened by F.A.O. have already assessed requirements of calories and protein.<sup>1,2</sup> A report on calcium requirements has now been published by a group of seventeen experts convened jointly by F.A.O. and W.H.O., with Professor F. G. Young, F.R.S., as chairman.<sup>3</sup> Calcium was chosen for early attention both because of its nutritional importance and because conflicting views have been held by different experts about the requirements necessary for health and growth. As the group points out more people fail to get the currently recommended allowance of calcium than of any other nutrient. In contrast, there is little evidence of specific disabilities attributable to lack of calcium in the diet. Danger might exist, therefore, of the diversion of effort and funds towards the correction of an imaginary deficiency. The possibility might even be visualized, and indeed has already been

emphasized by some, that an excessive intake of calcium may be not only unnecessary but also harmful.

In the diets of most countries, as tables at the end of the report show, only a few types of foodstuff can be counted as rich sources of calcium. In all those regions in which the dairy cow contributes substantially to human nutrition, the bulk of the calcium intake is obtained from milk and its products. Thus in Britain, Canada, the U.S.A., and most of the Scandinavian countries milk provides 75% or more of the dietary calcium. Green vegetables are another good source, but meat and unfortified cereals are poor sources. Fats and sugar provide calories with virtually no calcium.

For almost all nutrients experimental evidence about the exact amounts necessary to prevent the appearance of clear signs of deficiency is still scanty. Laborious feeding trials on human volunteers designed to find the requirements for vitamins A and C, for example, have given us only approximate answers about the intakes necessary to maintain health.<sup>4,5</sup> As to calcium, direct attempts to assess requirements appear to be limited to two investigations, in Peru and Norway, on small groups of prisoners.<sup>6,7</sup> Nutritionists therefore tend to be guided by the actual intake by healthy subjects in the countries in which they live, and to equate these intakes to the physiological requirements. Assessments of requirements reached in western countries, therefore, will be set at levels consistent with the high calcium content of cow's milk. A reasonable estimate of the requirement of the average adult on this basis can be taken as 1,000 mg. of calcium daily. Bovine milk, however, is five times richer than human milk in calcium. It is obtained in large quantities by the stimulation of lactation to an extent far beyond that demanded for the natural nutrition of the calf. The question may be raised, therefore, whether it is "natural" for western diets to contain so much calcium. May not the customary intake considerably exceed the minimum physiological requirement? The inhabitants of many eastern countries, not heavy milk drinkers, subsist on diets which give the average adult only about 400 mg. of calcium daily and which

<sup>1</sup> *Calorie Requirements*, F.A.O. Nutritional Studies, No. 15, 1957. Rome.

<sup>2</sup> *Protein Requirements*, F.A.O. Nutritional Studies, No. 16, 1958. Rome.

<sup>3</sup> "Calcium Requirements," *Wld Hlth Org. techn. Rep. Ser.*, No. 230, 1962, Geneva.

<sup>4</sup> *Vitamin A Requirements of Human Adults*, M.R.C. Special Rep. Series No. 264, 1949. H.M.S.O., London.

<sup>5</sup> "Vitamin C Requirement of Human Adults," *Spec. Rep. Ser. Med. Res. Coun. (Lond.)*, No. 280, 1953. H.M.S.O., London.

<sup>6</sup> Hegsted, D. M., Moscoso, I., and Collazos, C., *J. Nutr.*, 1952, **46**, 181.

<sup>7</sup> Malm, O. J., *Scand. J. clin. Lab. Invest.*, 1958, **10**, Suppl. 36.

<sup>8</sup> National Research Council, Reprint and Circular Series, No. 129, 1948. Washington, D.C.

<sup>9</sup> British Medical Association, *Report of the Committee on Nutrition*, 1950. London.

are not associated with any evidence of calcium deficiency.

The Expert Group had therefore to decide whether the calcium intakes of eastern nations really need to be raised to western standards, or whether the high intakes in western nations are in danger of being excessive. Broadly speaking both questions were answered in the negative. It was realized that the evidence is still inadequate for the accurate assessment of physiological requirements, but the following "suggested practical allowances" are put forward :

Age	Allowance (mg. per day)
0-12 months (not breast fed) ...	500-600
1-9 years ... ..	400-500
10-15 years ... ..	600-700
16-19 years ... ..	500-600
Adults ... ..	400-500

These recommendations allow for the greater calcium demands during growth than in maturity. No difference is made for sex, except that to meet the special needs of the third trimester of pregnancy and during lactation an allowance of 1,000-1,200 mg. is suggested.

By a surprising omission the assessments of calcium requirements reached by previous official committees are not quoted. The low level of the new allowances may be judged by comparing the 400-500 mg. now recommended for the average adult with the 1,000 mg. recommended in 1948 by the U.S.A. National Research Council.<sup>6</sup> At the same time the Expert Group "was not aware of any population study showing deleterious effects from an excessive calcium intake," and recognized the possibility that a high intake may be beneficial in the amelioration of senile osteoporosis.

Reference to the tables in the report shows that the calcium intake falls very slightly below the "suggested practical allowance" only in Italy, India, and Japan. Heavy fortification of eastern dietaries with calcium therefore appears to be unnecessary, but the high intakes of the western nations do no harm. So far as calcium intakes are concerned, a strong case seems to have been made out for "leaving well alone," and for the avoidance of precipitous action by W.H.O., F.A.O., or other official bodies.

In 1950 a Nutrition Committee sponsored by the British Medical Association commented on the paucity of the evidence then available about calcium requirements.<sup>9</sup> The F.A.O./W.H.O. Expert Group fully recognizes that our ignorance still continues, and urges the need for intensive research, particularly in the following fields: basic studies on the histology, biochemistry, and physics of bone in relation to age and growth; the collection and examination of

bones from different regions, especially those bones, such as the vertebrae, which have a high calcium turnover; the relationship between calcium intake and calcium balance and growth; thorough study of population groups habitually consuming very high or very low levels of calcium; the relationship between calcium intake and the level of calcium in the plasma and other plasma constituents such as proteins, which may be influential; the effects of different levels of calcium intake on health in repeated pregnancy and lactation; and the role of dietary calcium in the aetiology and treatment of osteoporosis. Readers of this interesting report, which also covers aspects of the problem too numerous for mention in a short review, will doubtless agree with these suggestions.

### IRON OVERLOAD

The chronic accumulation of excessive amounts of iron in the body is a serious danger and may be complicated by diabetes mellitus, heart failure, hepatic cirrhosis with congestive splenomegaly, and hepatoma. Any of these may cause death: the life expectancy in haemochromatosis after diagnosis is about one-sixth that of a healthy individual.<sup>1</sup> Although idiopathic haemochromatosis is the classical example of iron overload, the same pathological sequelae may complicate prolonged haemolytic states, thalassaemia, and aplastic anaemias, particularly if repeated blood transfusions are given.<sup>2</sup> In haemochromatosis the total body iron usually reaches values of about 40-60 g., and, although the accumulation of such quantities of iron would take some 20-40 years via the gastrointestinal tract, this time is greatly accelerated by parenteral iron therapy or blood transfusion, since the latter provides some 250 mg. of iron per 500 ml. of blood.

The treatment of idiopathic haemochromatosis has been greatly improved since the introduction of iron depletion by venesection. It is possible to deplete such patients of iron by weekly venesections for about two to three years until their stores are normal. Patients treated in this way remain well, and clinical evidence of iron overloading may recede.<sup>3</sup> This therefore remains a satisfactory form of treatment of this disease. Secondary haemochromatosis is more difficult to treat. Venesections are clearly contraindicated since anaemia is already present, and removal of iron must be procured by some other route. To this end attention has been turned to chelating agents, which might remove iron from the body in a soluble form via the urinary tract.

<sup>1</sup> Finch, S. C., and Finch, C. A., *Medicine (Baltimore)*, 1955, **34**, 381.

<sup>2</sup> Smith, C. H., et al., *Blood*, 1960, **15**, 197.

<sup>3</sup> Davis, W. D., and Arrowsmith, W. R., *J. Lab. clin. Med.*, 1952, **39**, 526.

<sup>4</sup> Fahey, J. L., et al., *ibid.*, 1961, **57**, 436.

<sup>5</sup> Bickel, H., et al., *Experientia (Basel)*, 1960, **16**, 129.

<sup>6</sup> Sephton Smith, R., *Brit. med. J.*, 1962, **2**, 1577.

<sup>7</sup> Bannerman, R. M., Callender, Sheila T., and Williams, D. L., *ibid.*, 1962, **2**, 1573.

<sup>8</sup> Moeschlin, S., and Schneider, U., *Proc. IX Internat. Congr. Haematol.*, 1962, Mexico.

<sup>9</sup> Pitcher, C. S., Williams, R., and Newman, F., *ibid.*, "