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Pointers

Neurological Damage in Parturition: Minor damage is not necessarily detected by classical neurological examination. Standardized quantitative observations are suggested to reveal handicaps and facilitate rearing these infants (p. 763). Leader at p. 761.

Obstetric Analgesia: Assessment by anaesthetist, patient, and midwife indicate that 0.35% methoxyflurane is suitable for intermittent self-administration during labour (p. 767).

Oral Contraceptives: Undesirable menstrual side-effects of microdoses of chlormadinone diminished by addition of oral oestrogens (p. 771).

Pneumoconiosis: Gas transfer defect of lungs found in 10 out of 16 patients whose radiopacities were of pure pinhead type, but in none of 11 men whose opacities were micronodular in type (p. 772).

Febrile Illness in General Practice: E.C.H.O. virus type 3 incriminated as causative agent in a geographical epidemic, which mainly affected children (p. 774).

Intermittent Claudication: Calf muscle denervation gave encouraging results in patients with inoperable femoropopliteal occlusions (p. 776).

Gynaecomastia: Observed in 6 patients with chronic renal failure during early stages of regular dialysis treatment (p. 779).

Pyloric Stenosis and Blood Groups: Lowered incidence of group A demonstrated in 303 patients with infantile hypertrophic pyloric stenosis. Salivary ABH secretor status showed no significant difference from controls (p. 781).

Case Reports: Ureterosigmoidostomy and neoplasia (p. 783); Nail-gun fatality (p. 784).

Congenital Heart Disease: Clinicopathological Conference at Royal Postgraduate Medical School (p. 785).

Upper Alimentary Bleeding: Surgical management (p. 790).

School Health Service: Trial of using general practitioners (p. 797).

Health Centres: Conference of doctors working in them (p. 800). Leader at p. 759.

Nursing Services in General Practice: Letters (p. 803).

Requests for Abortion: Said to be increasing (p. 802).

C.C.H.M.S.: Debates Welsh area health board plan (*Supplement*, p. 89).

Board of Science and Medical Education: Chairman of Council's proposals (*Supplement*, p. 92).

Public Health Pay Dispute: Agreement reached (*Supplement*, p. 94).

Cardiac Transplantation

On 3 December Professor Christian Barnard and his colleagues replaced the heart of 55-year-old Louis Washkansky with that of a 25-year-old girl mortally injured in a road accident. On 21 December Washkansky died, apparently from pneumonia. It is worth noting that the rejection process itself can cause pulmonary disease, but according to press reports the disease was infective in the present case. After a necropsy showing that death was due to pneumonia Professor Barnard was reported[1] as saying that there was no clinical evidence to suggest that rejection played a part in the death, and there was no evidence for human heart transplants to be discontinued. Despite its sad conclusion this was an outstanding surgical feat by the staff of the Groote Schuur Hospital at Cape Town. It was the application to man of a technique which had before been tested in animals and was a courageous operation that was bound to be attempted sooner or later.

How do the problems differ from those of the transplantation of kidneys? Successful matching of the tissues of the donor and the recipient is much more crucial for transplantation of the heart than of the kidney. The kidney is a complex structure, but its function is secretory and a fraction of its potential function will suffice for life. The heart is a unique organ; its vital activity must not falter for more than minutes and there is no artificial substitute which can preserve life for more than a matter of hours. Ischaemic damage may be incurred during transfer of a kidney, but recovery of such tubular necrosis may be confidently awaited. Meanwhile the artificial kidney takes over. A rejection crisis may be surmounted in the same way. Even total failure of function leaves the patient little worse off, for he can return to the intermittent dialysis which had preserved his life before operation, and further kidney grafts can be attempted later.

The heart is a richly innervated organ, but transplantation brings about complete extrinsic autonomic denervation, resulting in near total loss of the myocardial stores of catecholamines.[2] If the heart is removed from a dog and then replaced (autotransplantation) this denervation may be only temporary, and signs of reinnervation may be found as early as 26 days after reimplantation. It has been shown that after one to three years the response to stimulation of the vagosympathetic trunk is normal, though the actual number of intact neural connexions is probably small if judged by the still depleted catecholamine content of the various chambers of the heart.[3] Reinnervation of hearts transplanted from one animal to another seems far less likely, and so the physiological consequences of chronic denervation of the heart have been extensively studied. The exercise tolerance has been shown to be nearly normal in animals with hearts surgically denervated by Cooper's technique,[4] and W. M. Daggett and his colleagues found that the work capacity of dog hearts 6 to 12 weeks after autotransplantation was remarkably close to that of normal hearts.[5]

Unlike the normal hearts which were studied, autotransplanted hearts utilized exogenous circulating catecholamines. This may be an important adaptation to cardiac denervation, for Daggett's team found no alteration in myocardial contractility after transplantation, though the weight of the heart increased, suggesting that its efficiency was reduced. The retention of fluid and the rise in blood volume which occur early after autotransplantation[6] are unexplained by these studies. This pseudo-heart-failure may be due to the loss of afferent vagal impulses from atrial stretch receptors and is easily countered by diuretics. Daggett has concluded that the autotransplanted and denervated heart achieves a similar level of performance to the normal heart and that total denervation of the heart, with its concomitant depletion of myocardial stores of catecholamine, does not preclude successful transplantation. Thus the main barrier to successful transplantation of the heart in man seems to be the question of rejection. Further advances will depend on either better immunosuppressive drugs or more probably the perfection of tissue-matching techniques, so that donor can be exactly matched to recipient.

Over the past two years leucocyte antigen groups have gradually been defined. Antisera obtained from multiparous women, patients who have had multiple transfusions, and recipients of skin and kidney allografts have been characterized and can be used to test for leucocyte-group compatibility.[7-9] So far no prospective studies have been reported, but a retrospective study of donors and recipients after renal transplantation between relatives has recently been carried out by F. T. Rapaport and his colleagues and has shown that there is a considerable correlation between good leucocyte-group compatibility and success of the graft.[10] The success of some kidney grafts despite apparent leucocyte incompatibility, and rejection of others despite apparent compatibility, underlines the fact that tissue typing is still in its infancy, but even at this stage the success of kidney transplants should become more predictable.

If tissue antigens do have some degree of overlap cardiac homotransplantation (from one person to another) will certainly be practicable. Furthermore, tissue compatibility may exist between different species, so that heterotransplants (between species) may become possible. This would solve some of the ethical and logistical obstacles to homotransplantation that have been discussed.

The diagnosis of death first became a problem with the use of elective cardiac arrest during cardiopulmonary bypass, for until then the issue had been simple : a patient was dead when the heart stopped. But it is the brain which determines whether life continues. If cerebral function has been destroyed the patient is really dead, and the artificial preservation of tissue integrity by a machine does not alter the fact. The difficulties stem from the need to know for certain whether cerebral damage is irreversible. Relatives of patients with irreparable brain damage have to give permission for organs to be removed, and it would be understandable if some at a time of great distress were hesitant over a request to remove a heart. The coroner's permission is also needed. The short period for which organs can be maintained in good condition outside the body greatly limits the possible scope of large-scale transplant surgery at present, but soon it will be possible to keep organs viable for up to 48 hours after removal, and organ banks will eventually be developed. Until that time there will inevitably be many more potential recipients than there are organs available. But during the next decade cardiac transplantation will probably begin to save lives.

[1] *The Times*, 19 December 1967.
[2] Cooper, T., Willman, V L., Jellinek, M., and Haerlon, C. R., *Science*, 1962, **138**, 40.
[3] Peiss, C. N., Cooper, T., Willman, V. L., and Randall, W. C., *Circulat. Res.*, 1966, **19**, 153.
[4] Donald, D. E., and Shepherd, J. T., *Amer. J. Physiol.*, 1963, **205**, 393.
[5] Daggett, W. M., Willman, V. L., Cooper, T., and Haerlon, C. R., *Circulation*, 1967, **35**, Suppl. 1, 96.
[6] Willman, V. L., Merjavy, J. P., Pennell, R., and Haerlon, C. R., *Ann. Surg.*, 1967, **166**, 513.
[7] Dausset, J., Ivanyi, P., and Ivanyi, D., in *Histocompatibility Testing*, Munksgaard, Copenhagen, 1965, p. 51.
[8] Rapaport, F. T., Lawrence, H. S., Converse, J. M., and Mulholland, J. H., *Ann. N.Y. Acad. Sci.*, 1964, **120**, 280.
[9] Van Rood, J. J., Van Leeuwen, A., Schippers, A. M. J., Vooys, W. H., Frederiks, E., Balmer, H., and Bernisse, J. G., in *Histocompatibility Testing*, Munksgaard, Copenhagen, 1965, p. 37.
[10] Rapaport, F. T., Dausset, J., Hamburger, J., Huone, D. M., Kano, K., Melville-Williams, G., and Milgrom, F., *Ann. Surg.*, 1967, **166**, 596.

Disease from Monkeys

Wild animals, particularly primates, imported either for sale as pets or for use in laboratories may introduce a wide variety of infections into Britain. A joint committee of the British Veterinary and British Medical Associations reviewed the problem in 1962, and a leading article in these columns[1] drew attention to the problem. The committee thought that legislation and proper quarantine arrangements to control the importation of wild animals (particularly primates) were essential, but that it would be necessary to collect more evidence of the hazard before a strong case could be made for official action probably requiring substantial public expenditure.

Occasional cases of herpes virus B encephalomyelitis due to monkey bites continue to be reported.[2] An imported monkey recently developed rabies in a laboratory animal house.[3] But lately serious outbreaks of infection in Marburg, Frankfurt, and Belgrade have at last focused more official attention on this problem in many countries. Vervet monkeys (*Cercopithecus aethiops*) were imported from Uganda through London, and the shipment was divided between laboratories in Marburg and Frankfurt. An acute febrile illness with rash, varying degrees of lung and liver damage, gastrointestinal disorders, and a tendency to bleeding associated with thrombocytopenia occurred in about 28 persons who had had contact with blood or tissue of these monkeys, and 7 of them died. There were a number of secondary cases in hospital staff with some sort of contact with the blood of patients. At about the same time similar monkeys were imported (some through London) to Belgrade. There two cases of the disease occurred: one a veterinarian who carried out necropsies on monkeys which had died in quarantine, the other his wife. A full report of the disease is to be published in *Deutsche Medizinische Wochenschrift*.[4]

Transmission in man seems to be by contact with infected blood or tissue, and a limited experiment[5] suggests that the agent may be able to pass through the skin. Thus on present evidence general spread of this disease from man to man is unlikely, but the risk of infection must be constantly borne in mind by those who work (or play) with recently imported monkeys and by medical and nursing staffs treating febrile illnesses in such people. In obscure febrile illnesses and especially in cases of encephalitis questions about contact with animals (especially monkeys) should always be asked.

Material from the German cases was sent to laboratories in various parts of the world, and the major investigation of the human material was carried out at the Microbiological Research Establishment, Porton, Salisbury, which has the best