properties such as the degree of binding of the drug to protein and its molecular size is essential.¹³

That intensive supportive therapy alone can produce results as good as if not better than when combined with active elimination has recently been shown by A. B. Baker²² in Brisbane. He reported on 553 patients unconscious from a variety of drugs in overdosage, with a mortality of 0·74% and a very low morbidity. In no case was any attempt made to speed up elimination of the drug. Figures from the Edinburgh Centre²⁴ also strongly favour intensive supportive therapy without active treatment except where it is clearly indicated. In the years 1967 and 1968 the mortality in 2,041 patients was 0·6%. Apart from acute salicylate poisoning, in which, of course, active measures are effective,²² they were required in only thirteen patients.

Though intensive supportive therapy has been mistaken for therapeutic nihilism, it is in fact the antithesis of inactivity. Best undertaken in a ward set aside for the treatment of poisoning,²⁸ it consists basically in the maintenance of vital functions.²⁷ Adequate respiration may be achieved simply by turning the patient on his side or inserting an oropharyngeal tube. Deeply unconscious patients will require cuffed endotracheal intubation. The tube may remain in situ for between 24 hours²⁵ and 72 hours²⁶ before tracheostomy, which is seldom required.²² An adequate assessment of respiratory function for practical purposes can be achieved by measuring the minute volume.²⁸ ²⁷ ²⁵ ²⁷ If it is less than 4 l. per minute, hand ventilation or a mechanical ventilator will usually be necessary. Blood-gas analysis is desirable in the management of severe respiratory failure. If the unconsciousness is associated with convulsions, as in poisoning by tricyclic antidepressant drugs, phenoxybenzamine, or methaqualone, then curarization and controlled ventilation may be needed.²⁹

Shock may be more rationally treated if the central venous pressure is monitored,²¹ but in practice if the systolic blood pressure is below 90 then the foot of the bed should be raised. There is some doubt about the relative merits of vasoconstrictor drugs or plasma expanders to combat shock.¹² If mephenesin (Aramine) is used—and it will generally be successful—5 mg intramuscularly repeated once or at the most twice at 20-minute intervals should be given. Shock resistance to these measures may be aggravated by hypoxia or acidosis. In these circumstances arterial blood-gas analysis is essential.

Gastric aspiration and lavage requires the use of a tube of adequate size—for example, Jacques 30 English gauge. Except in salicylate poisoning, worthwhile recovery of drug will be achieved only if the patient is seen within four hours of ingestion.¹² The patient’s lungs must be protected by either an adequate cough reflex or a cuffed endotracheal tube. Syrup of ipecacuanha and apomorphine are of uncertain value and may even be dangerous.³⁰

Cardiac failure should be treated by rapid digitalization. Arrhythmias, common in young patients suffering from overdoses of tricyclic antidepressants, should be countered with pyridostigmine, propranolol, or lignocaine.³¹ Hydration should be maintained by the infusion of 1,000 ml. 5% dextrose and 500 ml. normal saline in alternation over 24 hours, but it is usually unnecessary to give parenteral fluids unless the patient remains unconscious for more than 24 hours.

A successful outcome may well depend on the standard of nursing care. Hypothermia, unless very severe, ³² C (86° F.), should be treated in a warm room, and active reheating is to be avoided. Common errors in treatment, apart from employing active measures unnecessarily, are the routine use of antibiotics and analeptics and of bladder catheterization. But intensive supportive therapy alone is not always appropriate. For example, patients severely poisoned by phenobarbitone or barbitone should be given forced alkaline diuresis or dialysis.

The chances of an unconscious poisoned patient dying in hospital should be slim, but restoration of physical well-being is not the end of treatment. It should be only the beginning of the essential elucidation of why the patient poisoned himself.³³

Real Hearts . . .

From the experience of over 100 operations for transplantation of the heart, discussed recently in these columns,¹ it is clear that the main cause of failure has been the immune reaction against the implant. But it is worth noting that the results of kidney transplantation ten years ago were worse than the present results of heart transplantation.

The centre with the largest experience of heart transplantation is Houston, Texas, where D. A. Cooley and his colleagues have performed 17 heart transplants.² With the same immunosuppressive regimen that would allow survival of half the unmatched kidney grafts at one year the results at Houston of cardiac grafting are much inferior, despite surgical technique of the highest order. Cooley and his colleagues have shown that there is a correlation between tissue typing and survival of the grafted heart. They have found that when the tissue match is poor inexorable rejection is likely, and even large doses of immunosuppressive drugs may not prevent destruction of the heart. It is disappointing that the use of antilymphocyte serum has not been shown to prevent the rejection process in these cases. But since preparations of it vary greatly in their immunosuppressive potency and toxicity it is difficult to compare one product with another.

The morphological changes in the transplanted heart are like those seen in the kidney grafts—namely, interstitial infiltration with mononuclear cells, oedema, necrosis of the heart muscle, and—apparently the worst lesion—an insidious arteritis in which the endothelium becomes duplicated and fibrotic and the lumen of the vessel reduced or eliminated. This process leads to myocardial ischaemia and can appear clinically rather suddenly in a patient who appeared to be reasonably well—a clinical situation all too familiar in myocardial ischaemia due to coronary atherosclerosis. It has been suggested that a heart consisting mainly of muscle, a relatively simple structure, might not be particularly antigenic, but heart grafts are rejected by animals certainly as aggressively as kidneys; indeed, the process may be rather more severe with the heart. Organs differ in the likelihood of their rejection; experimental evidence suggests, for instance, that the liver is less likely to be rejected than the kidney.

The patient with acute, potentially reversible rejection of a grafted heart may be very difficult to care for during this critical phase, since there is no cardiovascular technique analogous to the use of dialysis to maintain a patient with poor renal function. The experience of the Houston workers would seem to be similar to that of others, and the conclusion they came to is that "human cardiac transplantation is still an investigative procedure with minimal clinical application." Probably cardiac transplantation should not be performed unless the tissue match of donor and recipient is good, since it is clear that present immunosuppression can cope only with a mild rejection process. How can a good tissue match be achieved with the present shortage of donors and the difficulty of maintaining a patient dying of heart disease? These problems may be resolved in the future. Perhaps better methods of immunosuppression will change the pattern of rejection even when the tissue match is poor. For the present it would seem justifiable to proceed cautiously with clinical cardiac transplantation in carefully selected recipients when a closely compatible donor heart can be used.

... and Artificial Hearts

Interest in the development of artificial hearts has been virtually confined to the United States. Research there has been along two lines—replacement of the entire heart and assistance to the left ventricle only. A device to help the left ventricle can be used only for the relief of temporary left ventricular failure, such as may accompany acute myocardial shock or states of low cardiac output after open heart surgery. In chronic heart failure the function of the right ventricle is depressed as well as that of the left, and any assistance to the left ventricle alone leads to overload of the right side of the heart. C. W. Lillehei and colleagues have shown that the artificial heart has to take the whole load of the circulation or it will remain ineffective. Attention is therefore now being centred on complete replacement of the heart with an artificial device.

The problems to be solved before the artificial heart becomes a practical long-term proposition include the development of a source of energy which is reliable and portable. Artificial materials must be used which are inert and do not change their characteristics after implantation in the body. The device must be able to cope with the body's changing physiological requirements. And means must be found of preventing haemolysis and thrombosis on the artificial material that is in contact with the blood.

The sources of energy that have been tried for driving an artificial heart include electricity and compressed air or liquid. Compressed air is at present the most favoured. In future nuclear energy may become a practical proposition; so may electrical energy produced by the deformation by ribs or diaphragm of piezo-electric crystals, a method that uses the biological energy already available inside the body. Silastic and natural rubber are today the most popular artificial materials. They are biologically inert, do not change their characteristics when implanted in the body, and can withstand prolonged pumping in vitro for up to four years. The ability of artificial hearts to cope with increases in venous return is still somewhat limited, but progress is being made in this direction. Haemolysis produced by these pumps is already well within the range that can be taken care of by the body's reticulo-endothelial system. Research into the production of nonthrombogenic surfaces such as G.B.H. (graphite benzalkonium heparin) is developing rapidly, and it has proved possible to bind heparin on to the surface of Silastic rubber.

Basically the artificial heart of today consists of two collapsible sacs made of natural or synthetic rubber, guarded by inflow and outflow valves and contained in an outer rigid housing. The inner collapsible chamber houses the blood and ejects it into the circulation when compressed air or liquid is pumped into the space between it and the rigid outer housing.

Electronic mechanisms convert compressed air from a main source into a flow pulsating at predetermined rates. It has been found that a rate of 80 per minute, with two-thirds of the time devoted to diastole, produces optimum function in the artificial heart, and the pressure delivered is varied by a computer in order to relate it to the atrial pressures. Devices in the driving mechanisms give rounded wave forms to the compressed air, because these have been found to produce a physiological arterial pulsation.

Calves have been kept alive and apparently normal for up to 50 hours after excision of their own hearts and replacement by an artificial heart. Recently an air-driven artificial heart was used by D. A. Cooley to keep a patient alive for 65 hours while awaiting a suitable transplant donor in Houston, Texas. This patient had undergone open heart surgery, after which the heart had failed to resume its function. Until these devices are developed further and are more reliable, this may well remain the only indication for the clinical use of artificial hearts.