a group of young heroin addicts together is likely to produce anything but chaos. Some experts[20] would favour using extended hospital stay as a sort of hostel care, with eventual placement in a family. Getting the addict back into work and a settled way of life is an immensely more difficult problem than drug withdrawal.

There is again a lesson to be learnt from the treatment of alcoholism. The Ministry of Health's 1962 memorandum[21] emphasized specialist inpatient psychotherapy, with relative neglect of outpatient services and of rehabilitation. Clearly what is needed for alcoholism—and every other variety of drug dependence—is an integrated treatment service. This implies continuity of care and continuity of relationship, seeing the patient through from first contact to final rehabilitation. Should not the Government plan for at least one such experimental "model service"—a model no doubt as much for the problems it would throw up as the problems it would solve?

Many aspects of the growing addiction to heroin need urgent examination. What, for instance, is the relationship between experimenting with "soft" drugs and addiction to heroin and cocaine? Will morphine take the place of heroin as control of heroin becomes more stringent? That dependence on amphetamines and barbiturates is also a growing problem must not be forgotten, and the L.S.D. cult casts its shadow.[22] What are realistic aims of treatment—cure or containment? Is the "stabilized" addict a myth except for the rare middle-aged addict of therapeutic origin, or can the young addict function socially on a carefully maintained dose? The social and psychological roots of addiction may to some extent be illuminated by American research,[23] but generalization from conditions in New York, with its Puerto Rican and Negro slums, to London with its subculture of psychologically disturbed adolescents would be misleading. These are perhaps the type of questions to be tackled by the Addiction Research Unit which the Minister proposes to establish at the Institute of Psychiatry. The impact of legislative policy will be continuously under review by the Standing Advisory Committee already in operation.

The next few years present a great challenge. The outbreak of drug addiction on this scale in Britain is a grave symptom of social disorder, and the ability to deal with the emergency demands alike intelligent central organization and the skills and energies of individual doctors and nurses. But it must never be forgotten that, while addiction has many of the features of a contagious disease necessitating determined control, every addict is a sick person deserving compassion and skilled medical care.

Mercurialism Extraordinary

Mercury in pure metallic form is reckoned to be non-poisonous. But it can maintain this happy state only if it is in a vacuum or in contact with ion-free water. When it is in contact with body fluids, either in tissues or in the alimentary or respiratory tracts, it slowly releases mercury ions, which block the sulphydryl radicle in many enzyme systems.

Elsewhere in the *B.M.J.* this week are reports of two remarkable cases in which metallic mercury was self-injected (pp. 340 and 342) and a report of a third case (p. 347) in which mercury gained entrance to an artery during the collection of blood. After a few days local inflammation and necrosis developed, with later evidence of more widespread damage, particularly to the kidneys. In one case this was fatal. An interesting observation was the widespread dissemination of the mercury, illustrating aptly a quality which earned for the metal its name "quicksilver."

During recent years there have been several instances of parenteral poisoning with metallic mercury which has gained entrance from its use to secure a gas seal in syringes employed to withdraw blood from cardiac catheters and intravascular needles. J. T. Buxton and colleagues[1] have described a technique whereby the risk can be avoided. It would be even better not to use mercury for this purpose. Well-fitting syringes, promptly capped after detachment, are entirely suitable. Even if a small bubble of air gains entrance to the blood, the effect it will have on the gas content of the sample is less than the technical errors of the analytical methods and, in the physiological sense, is negligible. To use mercury is to strain for a degree of precision on one point out of proportion to the theory and practice of the whole technique.

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Immunological Development and Antibody Deficiency Diseases

At birth the human baby is called upon to adapt himself rapidly from the highly protected intrauterine environment to an outer world swarming with pathogenic micro-organisms. In his Leonard Parsons lectures C. A. Janeway[1] discusses the complex means by which this is achieved and the clinical manifestations that result from maldevelopment of the immune mechanisms.[2]

The immune response consists of a cell-mediated component expressed as delayed-type hypersensitivity, and of antibody production. These two aspects are controlled by separate central lymphoid systems,[3] both derived from primitive mesenchyme but subject to their own developmental defects. In the chicken the thymus controls the small lymphocytes which mediate delayed-type hypersensitivity and homograft rejection, and the bursa of Fabricius in the hind-gut gives rise to lymphoid cells, which are the precursors of antibody-making cells.[4] In man this separation is much less clear-cut. The studies of R. A. Good and his school provide some evidence that adenoids, tonsils, and the lymphoid tissues lining the intestinal wall may be "bursa-equivalents,"[5] but it seems that in higher animals the thymus controls some aspects of antibody production as well as the ability to reject grafts.[6]

In the normal baby the thymus is fully developed at birth and the lymph nodes are well populated by thymus-primed small lymphocytes, though delayed hypersensitivity and skin reactivity reach maturity at 4–5 months of age. The spleen and gut lymphocytes are also well developed, but lymph follicles and plasma cells appear only after the baby is antigenically "challenged"—for example, by an infection—and antibody production is not fully effective until about 7–9 months of age. To overcome this the human baby receives immunoglobulins (IgG) containing many specific antibodies via the placenta from about the 5th month of foetal life, and these maternal immunoglobulins diminish after birth. The level is down to half at 28 days, so that the gradual catabolism corresponds with the baby's increasing antibody-making capacity. This protective mechanism[7] is not without its dangers. Firstly, the maternal immunoglobulins can carry

harmful isoantibodies, causing haemolytic disease.[8] Secondly, they can also transmit pathogenic autoantibodies, causing temporary neonatal thyrotoxicosis, myasthenia gravis, hypoparathyroidism, or thrombocytopenia in some cases when the mother has these diseases.[9]

A more dangerous state of affairs arises when the baby's central lymphoid systems fail to mature, giving rise to the immunological deficiency syndromes. No fewer than 20 syndromes have been listed by Good,[10] associated with immunological deficiencies which can occur either as congenital malformations or as acquired diseases. The antibody deficiency states appear clinically as repeated infections by many different organisms, including all the common pathogens and yeasts such as monilia and *Pneumocystis carinii*. The mildest form of antibody deficiency is the transient hypogammaglobulinaemia of infancy, in which the synthesis of immunoglobulins is merely delayed. This can lead to multiple infections from about 6 months to several years of age, which can be helped by treatment with gammaglobulin. In this context it is of interest that premature babies, perforce born with underdeveloped immune responses, thrive better when given injections of immunoglobulins.

The most severe form of arrested maturation of immunity is the Swiss type of antibody deficiency,[11] in which the thymus and the bursa-equivalents are atrophic. The disease is inherited as an autosomal recessive characteristic, and none of the affected children have survived beyond 2½ years in spite of attempts at thymus grafts. These children are unable to reject homografts; in one case 45% of the circulating lymphocytes were found to be maternal, and the male infant died with symptoms reminiscent of the runting seen in graft-versus-host reactions.[12] The best-known form of antibody deficiency is the Bruton-type.[13] It occurs in boys, and the thymus is normal though synthesis of immunoglobulin may be severely defective. These children can lead a normal life when treated with regular injections of gammaglobulin sufficient to maintain their blood concentration at around 200 mg./100 ml., a level below which infections tend to recur. A third type of immune defect is characterized by severe hypoplasia of the thymus-dependent lymphocytes but with normal formation of intestinal plasma cells.[14] The patients may have autoimmune symptoms, particularly Coombs-positive haemolytic anaemia and an imbalance in the production of the different immunoglobulin classes IgG, IgA, IgM, and IgD. Similar anomalies are known to occur in patients with thymic tumours.[15 16]

One of the most important developments in the study of immunological deficiencies is the link with autoimmunity on the one hand and malignant lymphomas on the other.[3 17 18] In ataxia telangiectasia,[19] a developmental disorder with dysglobulinaemia and antibody deficiency, a proportion of patients die of malignant lymphomas. A related disease, Bloom's syndrome,[20] is also associated with increased susceptibility to infection and malignancy. Immunoglobulin studies have not yet been reported, but a chromosomal anomaly characterized by breakages and rearrangements has been described[21] which links it to Fanconi's anaemia,[22] in which disease there is a bone-marrow aplasia rather like that seen in association with thymic tumours.[23] It is possible that some maldevelopment of the central lymphoid apparatus, possibly making the primitive thymic cells susceptible to viral attack, may account for the interrelations between thymic dysplasias and tumours, antibody deficiency states, autoimmunity, and malignant lymphomas.

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Prolonged Endotracheal Intubation

The treatment of respiratory difficulty by prolonged endotracheal intubation was first described by Sir William Macewen in 1880.[1] He used it to treat two patients with obstruction of the upper respiratory tract. Despite the obvious advantages of endotracheal intubation over tracheostomy in terms of the ease of its performance, it was long thought that the method needed to be applied with great caution because of the risk of severe or even permanent damage to the larynx. But there is now increasing evidence that in fact endotracheal tubes may be left in for days or even weeks without serious sequelae provided certain prerequisites are met. The special complications of tracheostomy,[2] such as pulmonary infection, haemorrhage, persistent fistulae, and tracheal stenosis, may be avoided, but endotracheal intubation does carry a risk of damage to the larynx, presents difficulties in the use of suction catheters, and perhaps is more unpleasant than tracheostomy for the patient.

The extent, therefore, to which prolonged endotracheal intubation is a satisfactory alternative to tracheostomy depends on a careful assessment and comparison of the drawbacks of each. In studying the effect of prolonged intubation on the larynx J. P. Tonkin and G. A. Harrison[3] found in a series of 166 patients that the incidence of severe laryngeal trauma was 4.2%. Though the incidence is higher than in any other published large series,[4] the severe changes were not followed by any major permanent damage to the larynx so long as the period of intubation lasted no longer than 48 hours. Consequently these authors concluded that at least

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