ported that some of the patients with monkeypox, none of whom had previously been vaccinated, gave an equivocal reaction to smallpox vaccine, a finding which would be expected from a closely related vaccine strain.\(^5\)

Laboratory studies on the viruses so far isolated show that monkeypox strains are homogeneous but can be distinguished from other poxviruses by various laboratory tests. They appear to be more closely related to variola than to vaccinia or cowpox viruses.\(^6\) Further virological studies from the Congo disclosed the existence of monkeypox viruses in one clinically normal cynomolgus monkey and one normal chimpanzee, and further serological surveys for antibody to monkeypox in West and Central Africa have so far failed to detect any significant source of monkeypox virus infection.\(^7\) The true identity of these apparently rare cases might never have come to light but for the smallpox surveillance programme, and though the existence of a non-human reservoir of smallpox is possible the likelihood of this on present evidence seems remote.

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**Functions of Thymus-dependent Lymphocytes**

Though lymphopoiesis was observed in the thymus early in the present century, a role for this organ in immunity was established only in 1961. J. F. A. P. Miller\(^1\) found that thymectomy of newborn mice led to depletion of circulating lymphocytes, failure to reject foreign skin grafts, and early death from infection.

Congenital absence of the thymus and parathyroid glands in man, apparently resulting from a failure in development of the third and fourth pharyngeal pouches, was described in 1965\(^2\) and has been seen several times since then.\(^3,5\) In all of these conditions there is severe impairment of cell-mediated immune functions, including delayed hypersensitivity, contact sensitivity to dinitrofluorobenzene or other chemicals applied to the skin, rejection of foreign grafts, and capacity for a graft-versus-host reaction. In addition, children with defective function of the thymus show increased susceptibility to infections with certain viruses such as vaccinia, herpes simplex, and measles, or bacteria such as the Calmette-Guérin bacillus (B.C.G.) and to chronic mucocutaneous candidiasis. The selective depletion of thymus-dependent (or "T") lymphocytes, as in these conditions, contrasts with sex-linked hypogammaglobulinaemia, in which T lymphocyte functions are normal, and with stem cell defects, in which both types of immune response are defective (the so-called Swiss type of agammaglobulinaemia).

Some lymphoid stem cells arising in the bone marrow migrate to the thymus and differentiate into thymus-dependent or T lymphocytes. These cells have little, if any, immunoglobulin on their surfaces and do not secrete immunoglobulin. However, they have certain antigens which are absent from other lymphocytes. These antigens and chromosome and radioactive markers have facilitated studies of lymphocyte-migration.

Thymus-dependent lymphocytes circulate through blood and lymph to the so-called thymus-dependent areas of lymph nodes, spleen, Peyer's patches, and other lymphoid aggregates. T lymphocytes have relatively long lives (months or years) and constitute the bulk of recirculating lymphocytes. Each antigen specifically stimulates those T lymphocytes with receptors for that antigen, but not other T lymphocytes. Substances that stimulate mitosis, such as phytohaemagglutinin, stimulate T lymphocytes, irrespective of their specific receptors for antigen, but they do not stimulate other types of lymphocytes. This sort of stimulation results in increased synthesis of RNA and protein in the

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Radiation Safeguards

A deal o’ rich confused feedin’—the Scotsman’s judgement on the sheep’s head—might aptly be applied to the World Health Organization’s summary of arrangements for radiation protection.\(^1\) No environmental problem has ever been taken so seriously as the radiation hazard. Not surprisingly, the resulting pattern of regulations and advice is complicated.

Though dangers to staff and patients were recognized fairly early in the development of radiology, control measures were generally established by authoritative unofficial bodies. After the arrival of atomic energy in 1945 many countries introduced legislation, which inevitably overlapped existing codes of practice. During the past 25 years a measure of uniformity has been achieved in some directions through the activities of the International Commission on Radiological Protection. Most countries have adopted the commission’s view that the maximum permissible dose for radiation workers should be 5 rems per year for the whole body, with relaxations for exposure limited to the skin, limbs, or other limited regions.

The methods of enforcing these regulations—and of ensuring the safety of patients—vary considerably among the 19 countries included in the new W.H.O. survey. In France, California, and the Netherlands physicians must have special training before being licensed to use radioactive isotopes for diagnostic purposes. In Switzerland chiropractors are allowed to use diagnostic x-ray equipment after passing a test of competence. In West Germany regulations for the surveillance of industrial radiation workers are relatively strict, but there are no legal restrictions on the use of radiation or isotopes in medicine; physicians have “complete freedom of choice regarding the nature of the radiation to which they expose their patients for diagnostic or therapeutic purposes.”

The British system is in principle rather similar, since the codes of practice governing medical, dental, and veterinary practice have no legal force; nor has the advice of the Medical Research Council’s Isotope Advisory Panel. In practice, the educated concern of responsible professions is a better safeguard than detailed legislation.
T lymphocytes, followed by DNA synthesis and cell division. After division clones of cells stimulated by antigen become small again, recirculate, and can have a rapid secondary response on re-exposure to the antigen.

Exposure to antigen also causes T lymphocytes to liberate a series of products that affect the functions of other cells. Included in the products are a macrophage chemotactic factor, a macrophage migration inhibitory factor, a macrophage aggregation factor, lymphokotin (which kills certain other cells), and interferon. These products can reproduce many of the features found in delayed hypersensitivity lesions, including macrophage infiltration. As a result of cell-mediated immune reactions macrophages show increased capacity to kill intracellular organisms such as Listeria monocytogenes.

A second lineage of lymphocytes is now recognized and known as B lymphocytes. They have immunoglobulin (antibody) on their outer membranes, and respond to antigen by transforming into antibody-secreting cells. Most antigens, such as foreign proteins, stimulate B lymphocytes only inefficiently by direct contact. A second signal produced by interaction of nearby T lymphocytes with antigen is required for stimulation of B lymphocytes to proliferate and transform into antibody-secreting cells. Thus most antigens are thymus-dependent. But some naturally occurring antigens, such as pneumococcus polysaccharide or bacterial endotoxin, stimulate B lymphocytes as well as in the absence as in the presence of T lymphocytes; they are therefore known as thymus-independent antigens.

The functions of T lymphocytes can thus be defined as participation in various types of cell-mediated immune reactions and helping in the formation of antibody. The importance of T lymphocytes is evident from the severity of the syndrome of selective thymus deficiency. Because this defect allows the retention of grafted cells, attempts have been made to restore immune function by intramuscular inoculation of foreign fetal thymus cells. Cells from fetuses 13 to 16 weeks old have been used to reduce the danger of graft-versus-host reactions, which can be fatal after inoculation of thymus cells from stillborn babies or older persons. The children with grafted thymuses have had their T lymphocyte activities restored and been clinically improved.

Some degree of immunological reconstitution of thymectomized mice can be achieved by inserting into them thymus cells enclosed in diffusion chambers with pores too small to permit emigration of cells but large enough to allow release of secretory products. R. W. Steele and his colleagues have enclosed 13-week-old fetal thymus in a diffusion chamber in a child with thymic aplasia. The child's lymphocytes became responsive to phytohaemagglutinin, but she died 9 days after the graft. Though these results are compatible with the interpretation that a humoral thymus factor can bring about maturation of T lymphocytes in man, other effects cannot be excluded. In any case, injection of thymus cells is much more likely to restore immune function than enclosure of cells in a diffusion chamber, and it is to be hoped that, as these cases are recognized and treated, further experience of injecting fetal thymus cells will be gained.

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**Care of the Dying**

Even if there is some truth in the assertion that death has replaced sex as the taboo subject in our society at least doctors still recognize that it is one of their major concerns. Indeed, the last few years have seen growing medical interest in the case of the dying: the creation of hospices for terminal care; better understanding of the special psychological needs and problems at this time; and the realization that such care also involves continuing support of the bereaved. Nevertheless, clearly there is still much room for improving these services and on 29 November 1972 the Department of Health held a nationwide symposium on the subject. At page 29 of this week's B.M.J. we print shortened versions of the papers read at the symposium, which will be published in full by the D.H.S.S. together with the discussion.

Three main themes emerged from these contributions. Firstly, despite recent developments and the fact that many patients still die peacefully at home, we need many more specialist terminal-care units—possibly, according to one speaker, 12 beds for every half million people. Secondly, we need to continue to examine alternative ways of providing accommodation for the dying. In some areas the best solution is to provide long-term units attached to special or general hospitals or totally on their own. In other areas short-term units may admit the patient for further treatment, to relieve the strain on the family temporarily, or in the final stages. In yet others a few beds in a community hospital enable death to be placed in its proper perspective of the cycle of life from which many townsmen have become all too isolated.

The final main theme of the conference was the importance of team work in terminal care. Today the concept of the team seems to be a cliché brought out all too often in discussing any medical problem. But in the care of the dying undoubtedly a team led by the family doctor which includes district nurses, members of the social services and voluntary organizations, and the clergy has a valuable supportive role; and it should be easier to assemble teams like this after the forthcoming reorganization of the health services. Perhaps in no other field of medical treatment are minor details so important as in terminal care, and doctors will find many of the points raised at the admirable D.H.S.S. conference of great value.

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**Perinatal Therapeutics and Toxicology**

Any substance in solution in the blood of a pregnant woman can pass into the blood of the embryo or fetus. The question is not whether but how fast and by what mechanism any particular substance crosses the placental "barrier" and, with increasing emphasis, how its effects on the offspring compare with its effects on the adult. The thalidomide disaster made it only too clear that its effects on the embryo, at least, may be very different. And it has long been known that analgesic and anaesthetic agents administered to the mother during labour not only cross her blood-brain barrier but also tend to cross the placental barrier, and so to depress the nervous system of the fetus, with potentially disastrous effects.

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