have short histories, very high levels of serum gastrin, profound hyperplasia of the gastrin-secreting G cells in the gastric antrum, and a normal pancreas. Patients with type 2 disease have longer histories, less extreme hypergastrinaemia, a normal population of antral G cells, but hyperplasia or frank tumour in the pancreatic islets. If this division proves to be correct, it has important implications for management, because patients with type 1 disease should be cured by a lesser operation than total gastrectomy. Indeed, such a patient has now been described. Vagotomy and antrectomy abolished his symptoms and his serum gastrin levels returned to normal within two months.[18] Another consequence of this new concept of the Zollinger-Ellison syndrome may be the recognition of a new type of gastric tumour arising from the antral G cells. C. M. S. Royston and his colleagues[19] have recently discovered an early infiltrating tumour in the resected stomach of a patient with the syndrome; the tumour cells contained gastrin and appeared to arise from antral G cells.

The Zollinger-Ellison syndrome is not the only clinical condition in which an islet cell tumour of the pancreas is associated with diarrhoea. In 1958 J. V. Verner and A. B. Morrison[20] described two fatal cases of severe watery diarrhoea with hypokalaemia in which non-β-islet cell tumours were present. The condition in these patients should not be confused with the Zollinger-Ellison syndrome, since neither peptic ulceration nor gastric hypersecretion occurred, and in fact achlorhydria is usual in the former syndrome, though not invariable. Though the diarrhoea may be severe enough to warrant the name of "pancreatic cholera,"[21] others prefer to call it the W.D.H.A. syndrome.[22] The letters refer to the main features of watery diarrhoea, hypokalaemia with acidosis, and achlorhydria. There has been speculation about possible hormonal causes, but E. Elias and his colleagues[23] have now produced evidence that the syndrome is caused by over-production of an enterogastrone—namely, gastric inhibitory polypeptide.[24 25] It therefore seems that the known syndromes associated with overproduction of intestinal hormones may represent only the tip of an iceberg of endocrine disturbance.

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Monkeypox

In 1967 the World Health Organization initiated a worldwide eradication campaign against smallpox. In that year 131,000 cases of smallpox were reported to the W.H.O. from 42 countries, though it was estimated that fewer than 5% of cases were being reported. In 1970 only 21 out of the 42 countries experienced smallpox,[1] and in several of them the infection had been imported. More recently at a conference in Kampala D. A. Henderson[2] stated that as far as Africa was concerned only two major endemic foci remained, the Sudan and Ethiopia, and there is every likelihood that these areas will soon be cleared. But in 1970 several patients with illnesses at first indistinguishable from smallpox were discovered in smallpox-free forest areas of West and Central Africa. The investigation of these cases, carried out by several collaborating laboratories under the auspices of W.H.O., provides a remarkable story.[3]

Between October 1970 and May 1971 a virus was isolated from some patients in West Africa which was later identified as monkeypox. This virus had first been identified by von Magnus[4] in 1958 during an outbreak of a vesicular eruptive disease among captive primates in Copenhagen. Monkeypox virus is now recognized as a member of the pox group of viruses, the other important members of which are variola, vaccinia, and cowpox.

The first six cases of human infection with monkeypox were identified in West Africa—four in Liberia, one in Sierra Leone, and one in Nigeria.[5] Five of the patients were children and one an adult. None of the six had been vaccinated against smallpox. After a prodromal illness of 2-5 days a diffuse vesicopustular eruption of varying intensity developed. The rash was peripheral in distribution; there was no cropping, but the lesions themselves were somewhat different from those seen in variola major or minor.[5] They were discrete, deep-seated, and contained fluid so viscous that it was hard to collect for virological studies. Three of the patients were severely ill, but all recovered. Virus was obtained from four of the six patients and was identified as monkeypox, and the other two were diagnosed by serological tests.

Three of the cases had occurred in an area which had been free of smallpox for at least a year, though 38% of local residents were classified as susceptible to smallpox by the absence of a history of, or scarring from, smallpox or vaccination. During an extensive surveillance of the districts 15 suspect cases of pox disease were identified, but all except one case of monkeypox were proved to be varicella or other infection by non-pox virus. Two of the patients with monkeypox had occasionally consumed freshly killed monkeys for food and others were observed to play with the viscera of freshly killed monkeys. But serological studies on monkey sera failed to produce any convincing evidence of poxvirus infection in monkeys. A further case has been reported from the Congo in a 9-month-old unvaccinated child, who recovered from that infection but died soon afterwards of measles.[6] One additional and severe case with an eruption more typical of smallpox in distribution has been identified in a rural forest area of East Nigeria.[7] It has also been re-

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.[8] 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.[9] 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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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.

[1] *Protection against Ionizing Radiation: A Survey of Current World Legislation*. Geneva, World Health Organization, 1972.

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