malignant properties and will grow progressively in a proportion of the hamsters into which they have been implanted.

Electron-microscopy of Infected Cells

Electron-microscopic studies have been made of tissue-culture cells infected with virus from a number of different sources: from the hamster kidney tumour, from one of the induced mouse mammary carcinomas, and from a (Gross) virus-induced leukaemia in a C3H mouse. Cells from cultures which showed typical cytopathic changes were collected after trypsinization, fixed with osmic acid, embedded in methacrylate, and sectioned in the usual way. The controls comprised uninfected cultures subsequently treated in the same way.

Independent of the source of the agent, the nuclei of the infected cells were found to contain particles ranging in size from 30 m μ to 40 m μ , round or slightly oval in shape and at times appearing to possess a less dense centre. Some cells had enormous nuclei filled with myriads of such particles which had completely replaced the normal structure. Occasional packed nuclei were seen to have an incomplete membrane as though the nucleus had burst. The cytoplasmic structure in such cells was not so abnormal as to suggest that the dissolution of the nuclear membrane was an artifact of fixation or inclusion.

The cytoplasm of infected cells also contained electron-dense particles, but there were far fewer particles in the cytoplasm than in the nucleus in the cells studied. Moreover, some of these particles were 50–60 m μ in diameter, and differed from the intranuclear particles in having an external membrane surrounding a central body; the latter closely resembled the intranuclear particle. Examples were found in which the cytoplasmic particles appeared to be embedded in the cell membrane or in the membrane of cytoplasmic vacuoles. However, extracellular particles were also seen which were identical with those in the nuclei. No particles corresponding to those described above have yet been seen in control cultures, and we infer that the particles are associated with infectivity.

The dimensions of the intranuclear particles correspond to those given by Kahler *et al.* (1959) for polyoma virus in purified preparations. Similar intranuclear particles have been seen by Banfield *et al.* (1959) in thin sections of cells from cultures infected with polyoma virus. Extracellular virus-like particles have also been described by McCulloch *et al.* (1959) in some parotid-gland tumours that arose in Swiss mice after the inoculation of an agent derived from a C3H mouse mammary carcinoma.

We are trying to correlate the high infectivity of the medium from infected cultures with the number and type of particle found by electron-microscopy. We are also studying the developmental cycle of the virus in the cell, and, despite the apparent low yield of virus in the hamster tumours, are searching for characteristic particles in the tumour cells.

Summary

A virus, which we have called "M.H. polyoma," with properties similar to Stewart and Eddy's "polyoma" virus has been isolated in tissue culture from the spleen of a leukaemic AK mouse. When inoculated into suckling mice, rats, and hamsters, the virus produced a variety of tumours and other lesions. Some of these

tumours—renal sarcomata in hamsters and a mouse mammary carcinoma—were serially transplantable. In the hamster tumours the presence of the virus was only revealed by infecting tissue cultures of mouse-embryo fibroblasts. Electron-microscopy of infected tissue cultures showed many particles 30–40 m μ in diameter in the cell nuclei, and fewer, larger particles, with external membranes, in the cytoplasm.

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LYMPHADENOGRAPHY: ITS USES IN HAEMATOLOGY

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[WITH SPECIAL PLATE]

Lymphangiography by direct injection of contrast media into the lymphatics was performed as early as 1932 by Shdanow and by Menkes, but the idea remained unused clinically for 20 years, until Kinmonth (1952) described how a colloidal dye injected subcutaneously is picked up by the local lymph vessels, which thus become visible and can be surgically exposed for the introduction of an opaque medium and subsequent radiography. This technique was later improved upon by Kinmonth and co-workers so that the clinical application of lymphangiography became a relatively easy procedure (Kinmonth and Taylor, 1954, 1955). Kinmonth's team used the new method to investigate mainly disorders of the lymphatics (Kinmonth and Taylor, 1957).

Microlymphangiography and stereolymphangiography are but two examples of recent interest in this field (Bellman and Odén, 1957; Odén *et al.*, 1958), which, however, tends to refer chiefly to lymphatic vessels, as its name also implies. No work that we are aware of has utilized Kinmonth's technique in order to study the radiological findings from lymph glands (lymphadenography) in haematological diseases known to affect the lymphatic system.

The purpose of the present investigation was to visualize by radiography not simply the lymph vessels but mainly the lymph glands in several haematological diseases.

B. MALAMOS *ET AL.*: LYMPHADENOGRAPHY IN HAEMATOLOGY

FIG. 1. — Normal inguinal glands.

FIG. 2.—Inguinal glands in chronic lymphocytic leukaemia.

FIG. 3.—Inguinal glands in chronic myeloid leukaemia.

FIG. 4.—Inguinal glands in acute leukaemia.

FIG. 5.—Inguinal glands in lymphosarcomatosis.

FIG. 6.—Inguinal glands in lympho-granuloma (Hodgkin's disease).

FIG. 7.—Axillary glands in lympho-granuloma (Hodgkin's disease).

I. M. BRECKENRIDGE *ET AL.*: STRESS ULCERS IN STOMACH

FIG. 1.—Case 1. Section from pyloric antrum, showing typical acute ulcer confined to mucosa. (H. and E. $\times 7.5$.)

FIG. 2.—Case 5. Edge of acute ulcer in pyloric antrum, showing recent necrosis and almost complete absence of cellular infiltration. (H. and E. $\times 60$.)

Material and Methods

The method was used on 40 patients (34 males, 6 females) aged from 19 to 87 years. Ten of them were used as normal controls, since they were admitted to hospital for other than haematological diseases and showed no lymph-gland enlargement. The remaining 30 cases were suffering from lymphogranuloma (12 cases), chronic lymphocytic leukaemia (7 cases), chronic myeloid leukaemia (1 case), acute leukaemia (6 cases), and lymphosarcoma (4 cases). The diagnosis was confirmed by blood and bone-marrow examinations, puncture of the glands, as well as by histological examination of excised glands.

The method used can be summarized as follows. The patient was first checked for special sensitivity against "urografin" solution (76%). Then 0.5 ml. of patent blue violet ("patentblauviolett") in isotonic 11% solution was injected. The site of the injection was on the dorsal surface of the hand (5 cases) or foot (35 cases). After half an hour to two hours the hypodermic lymph vessels had become visible as blue lines, starting from the injection point and mounting up to the knee or elbow. After local procaine hydrochloride anaesthesia, a small incision (0.5–1 cm.) was made and a lymph vessel exposed. Then, with a very fine needle, the opaque medium (urografin, 76% solution) was injected at a rate of 1 ml. per minute up to a total of 4–6 ml. At the end of the injection the lymph glands of the area were seen fluoroscopically, and x-ray films were taken.

In two cases a fine polyethylene catheter was inserted into the lymph vessel. This procedure is of importance, not for the above diagnostic injection of opaque medium, but for eventual therapeutic injections into the vessels.

Results

The normal radiographic appearance of the inguinal or axillary glands after injection of an opaque medium into a lymph vessel of the foot or hand respectively is shown in Special Plate Fig. 1. The small size, the regular contour, and the equal density of the shadow all over the gland can be regarded as the main features of its normal appearance. In older patients the contour of the gland may on occasion not be so regular, though the other characteristics remain normal. Two cases of tuberculosis of the glands of the neck showed normal inguinal glands.

All 30 cases with neoplastic haematological diseases showed abnormal x-ray films of the lymph glands. In fact, 20 of these cases showed an irregular distribution of the density within the gland. Twenty-one cases had an irregular contour with defects at the border of the gland shadow. In 15 cases the defects were multiple, so that the gland had a "worm-eaten" appearance. These changes were observed on the examined inguinal or axillary glands (Special Plate, Figs. 2–7), even when these glands were not enlarged on palpation. The method gave positive results even in cases without abnormally enlarged lymph glands in any accessible gland group of the body. On the other hand, it should be noted that acute leukaemia and lymphogranuloma showed the most marked changes; however, the difference was only quantitative, and in our cases there was no definite sign that could differentiate with certainty between these malignant haematological diseases.

B

Discussion

Lymphadenography is a new method that can help in the diagnosis of certain diseases which affect the lymph glands. The main use of the method is to help distinguish between benign and malignant lymph-gland diseases. In normal cases the glands are small, with regular contour and equal density. In malignant diseases they may be larger, but they are irregularly outlined, often with one or multiple defects at the border of their shadow, a "worm-eaten" appearance, and an unequal density in several parts of the gland.

Up to now this method has not given any false-positive or false-negative results. Attention should be paid, however, to aged patients, in whom the gland contour can be found irregular in normal cases. It is of interest that a positive result can be obtained even if the glands are not considered abnormal on palpation. Such a positive result was thus obtained in two cases with splanchnic lymphogranuloma, without any peripheral-gland enlargement. In cases without peripheral-gland signs and without conclusive blood findings, lymphadenography can be regarded as of particular importance in establishing the diagnosis. On the other hand, the method cannot help in differentiating with certainty between several malignant haematological diseases, as was hoped (Fischer, 1957). Some difference was observed in cases of acute leukaemia and lymphogranuloma, where the changes were more marked than in the other cases studied in our series.

No side-effects were observed during the application of this method, except a transient pain felt by a few patients during the injection of the opaque medium.

Catheterization of the lymph vessels is a difficult procedure, and was achieved in only two cases. It is mentioned only because it may prove helpful in local therapeutic applications—that is, for direct injection of drugs into the lymph vessels and the lymph nodes of the area.

Summary

The radiographic visualization of the inguinal and axillary lymph glands was obtained in 10 patients with no lymph-gland enlargement and in 30 with diseases involving the lymphatic system.

Characteristic changes were observed in all cases with malignant haematological diseases, such as leukaemia, lymphogranuloma, and lymphosarcoma. It is suggested that the method could be of great help in cases lacking apparent involvement of the peripheral lymph glands.

Lymphadenography cannot as yet differentiate with certainty between leukaemias, lymphogranuloma, and lymphosarcoma.

There are no important side-effects in the clinical application of lymphadenography.

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