larger doses used. However, experiments with animals have demonstrated that neosynephrine does not produce ventricular fibrillation even in relatively high doses in animals sensitized by cyclopropane anesthesia.[6] If a given dose is ineffective, a larger dose may be given after a 10-minute interval until the rhythm is reverted or until a rise of systolic pressure up to about 160 mm of Hg is produced. Doses between 0.5 mg and 1.0 mg should be effective in most cases.

Two of the 4 patients complained of mild precordial discomfort for a few minutes following the injection. This was the only unpleasant effect noted. Each patient described either a sensation of coolness of the skin or a tingling sensation evidently produced by the cutaneous vasoconstriction and piloerection.

Summary. Four nonhypertensive patients with idiopathic paroxysmal tachycardia of supraventricular origin were given neosynephrine intravenously in amounts sufficient to increase the systolic blood pressure 30 to 40 mm of Hg. In 2 of these the attacks had persisted for several hours in spite of all mechanical methods of treatment and administration of mecholyl. In all 4 cases the rhythm reverted to normal within one minute after the injection of neosynephrine. This is considered to be produced by reflexes from the carotid sinuses and aortic arch. Occasional ventricular beats occurred during the 2-minute period after the return to the normal sinus rhythm. Blood pressure returned to normal within 4 to 8 minutes after the injection.

Intravenous injection of neosynephrine or some other brief-acting vasopressor compound may prove to be the treatment of choice in selected cases of auricular or nodal paroxysmal tachycardia.

[6] Meek, W. J., *Harvey Lect.*, Ser. XXXVI, 1940-41, 188.

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Dark-field Observations on Lymphocytes Exposed to X-Rays and Other Injurious Agents.*

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By the method of unstained cell counts, it has been shown[1,2] that X-rays had a delayed cytocidal action on lymphocytes irradiated *in vitro* and incubated at 37°C. The death of the cells was preceded by irregularities in the shape and the refractivity of the cells. In the present study, these morphologic changes were studied by dark-field illumination with a cardioid condenser.

On dark-field examination of a fresh suspension of the thymus of a rabbit, most cells appeared filled with fine intranuclear granules and a few cytoplasmic mitochondria (Fig. 1). After irradiation of the suspension and incubation for 3.5 hours, about 32% of the cells developed one or a few small, dark, round structures which may be termed primary vacuoles (Fig. 2). On dark-field examination, it was not possible to determine whether these structures were in the nucleus or cytoplasm. The vacuoles occasionally increased in size during observation. Some of them were surrounded by thick, bright, circular walls. They caused the distortion of the shape of many cells. They were present in viable cells which resisted staining with

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[1] Schrek, R., *Radiology*, 1946, **46**, 395.

[2] Schrek, R., *J. Cell. and Comp. Physiol.*, 1946, **28**, 277.

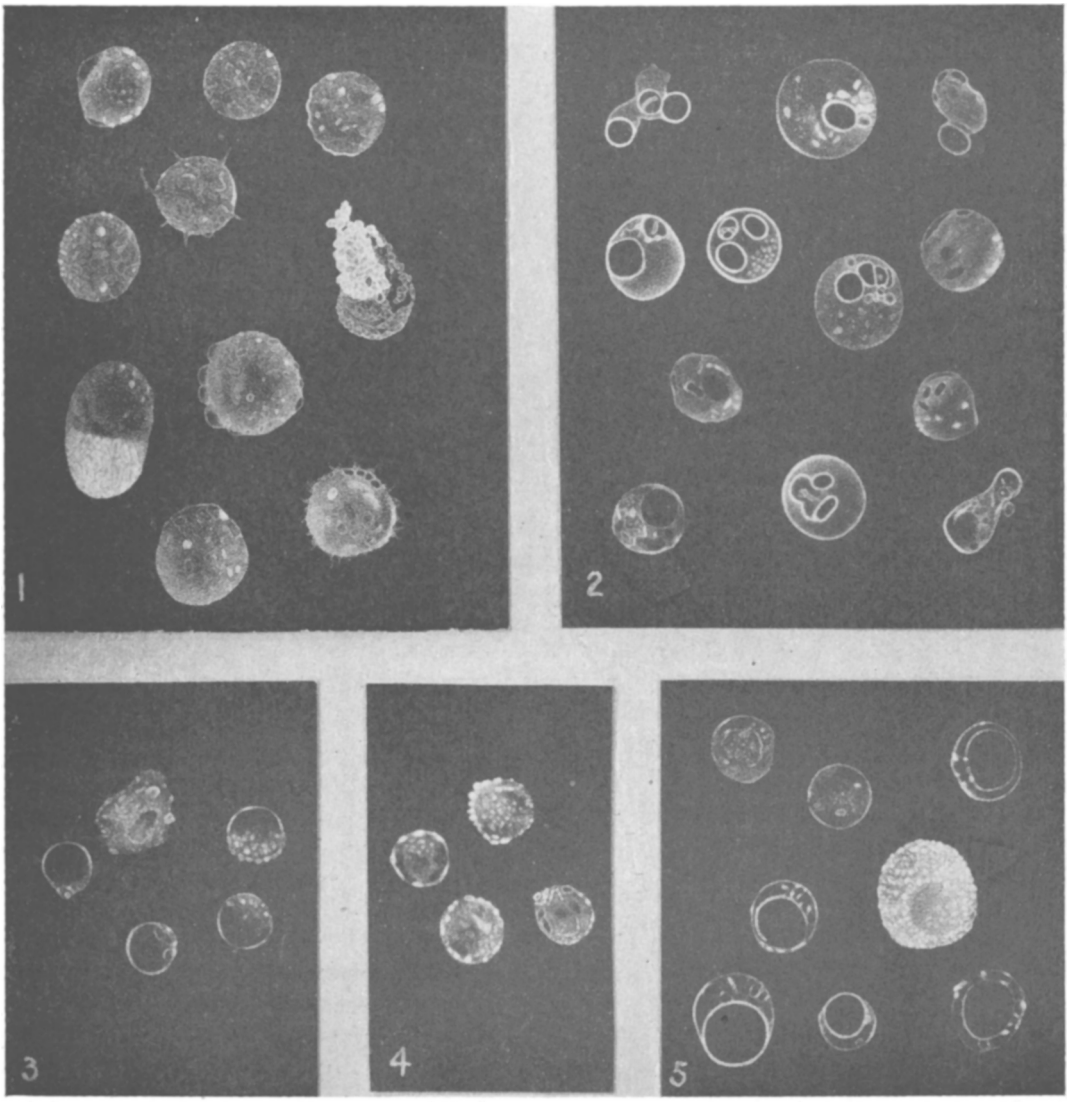

FIG. 1. Cells in a suspension derived from the thymus of a rabbit. The cells have innumerable fine intranuclear granules and a few larger mitochondria. A few cells show degenerative changes—small cytoplasmic bullae and thin cytoplasmic projections. Two granulocytes are shown.

FIG. 2. Thymic cell suspension, radiated (1000 r) and incubated for 3 hours at 37°C. The cells have one or more primary vacuoles, some of which are surrounded by bright vacuolar walls. A few cells are distorted.

FIG. 3. Thymic cell suspension, radiated (1000 r) and incubated 24 hours at 37°C. The cells are small, have relatively large secondary vacuoles and crescents of small and large granules. The cell walls are distinct. One normal granulocyte is present.

FIG. 4. Thymic cell suspension incubated for 3 hours at 45°C. The cells are small with fine and coarse granules.

FIG. 5. Thymic cell suspension treated with an equal volume of distilled water. The nuclei are dark, free of granules and have a distinct nuclear wall. The granulocyte appears normal.

Magnification in all figures is 1250 ×.

eosin. The spherical vacuolated cells had a greater average diameter than the non-vacuolated.

In histologic sections of the suspension, approximately 12% of the nuclei had large, acidophilic or slightly basophilic, Feulgen-

TABLE I.
A Comparison of the Characteristics of Primary and Secondary Vacuoles.

Method of study	Primary or early vacuoles	Secondary or late vacuoles
Dark-field examination		
Cell	Round or irregular	Round
	Usually increased in size	Usually small
	Usually no cell wall	Cell wall present
Vacuole	Single or multiple	Single
	Small or large	Relatively large
	Usually have vacuolar wall	No vacuolar wall
Histologic section	Intranuclear acidophilic area	Pyknotic nucleus
Method of unstained cell count	Usually in viable cells	In dead cells

negative vacuoles surrounded by dense chromatin material in the shape of a ring, horse-shoe or crescent. The intranuclear vacuoles in histologic sections correspond to the primary vacuoles observed on dark-field examination.

Similar vacuoles were observed both on dark-field examination and in histologic sections of rat thymic tissue excised 3 hours after irradiation *in vivo*.

On dark-field examination of a suspension irradiated *in vitro* and incubated 24 hours, 86% of the cells were small, had a thick, bright cell wall and a crescentic, polar mass of fine and coarse granules. Each of the cells also had a single, relatively large, round or oval, dark structure which was termed a secondary vacuole (Fig. 3). Cells with secondary vacuoles stained readily with eosin and were evidently dead. In stained sections, most cells had pyknotic nuclei which corresponded with the secondary vacuoles seen on dark-field examination.

A comparison of the primary and secondary vacuoles is given in Table I. It was usually possible to differentiate the 2 types of vacuoles on dark-field examination but intermediate forms were sometimes observed.

Nonirradiated suspensions incubated at 37°C also developed cells with primary and secondary vacuoles, but the rate of formation of the vacuolated cells was much slower. Apparently, irradiated and nonirradiated cells incubated at 37°C were killed by the same mechanism but irradiation accelerated the normal degenerative process.

In suspensions incubated at 45°C for 3 hours, the cells were dead and were filled with granules which appeared coarser and brighter than in the unincubated cells (Fig. 4). On histologic examination, many nuclei had large chromatin masses. The cells incubated at 45°C were apparently killed by a different mechanism (coagulation of protein?) than those incubated at 37°C. Furthermore, cytologic changes produced by heat were different from those induced by X-rays.

Irradiated cells incubated at 45°C appeared morphologically identical and survived as long as nonirradiated ones. Radiation did not accelerate the cellular degenerative processes at 45°C.

In view of Failla's[3] theory that X-rays cause the absorption of water into the nucleus, it is of interest to compare the effects of distilled water and of X-rays on lymphocytes. Addition of water to an equal volume of thymic cell suspension caused an immediate enlargement of the cells and a change in the nuclei which lost their granular appearance and became dark ill-defined areas (Fig. 5). Later the nuclear walls became visible as thin, bright lines. Histologic sections of thymic tissue incubated with water showed cells with vacuolated nuclei (Fig. 1 in Schrek[4]). In contrast, irradiated and incubated (37°C) cells in an isotonic solution suffered no morphologic change for 2 hours or more. After the latent period, there appeared small, dark, intranuclear vacuoles which enlarged and developed bright, vacu-

[3] Failla, G., in Ward, H. B., *Some Fundamental Aspects of the Cancer Problem*, The Science Press, New York, 1937, p. 202.

[4] Schrek, R., *Am. J. Path.*, 1945, **21**, 1101.

olar walls. Histologic sections showed vacuolated nuclei.

From the reports in the literature and the findings in this laboratory, it is possible to formulate a hypothesis on the action of X-rays on lymphocytes. Presumably, the radiation produced, in one or more foci in the nucleus, first a photochemical change, then a chemical reaction which caused the absorption of water into these foci with the formation of primary vacuoles. The vacuoles enlarged forcing the chromatin material peripherally. The ring of chromatin ruptured at one point and then contracted resulting in a horseshoe shaped mass, a crescent and ultimately a small, round pyknotic nucleus.

Summary. Incubation of lymphocytes in suspension at 37°C produced primary and secondary vacuoles visible on dark-field examination. Preliminary irradiation of the suspensions greatly accelerated this process. The addition of distilled water to lymphocytes produced enlargement and vacuolization of the nuclei. The hypothesis is proposed that irradiation caused the absorption of water into one or more foci in the nucleus.