it happen that Chadwick discovered the neutron? He knew from Compton's work what a photon would do if it struck an atom. He knew from long-established principles what an atom would do if it struck another atom. He could identify atoms by their ranges from the abundant data established by the long labors of Rutherford, Blackett, and himself. He possessed a great fund of knowledge and experimental skill, and he was a tremendous worker. Would he have been helped or hindered by a lot of clock punchers? I think it is of vast importance that we impress every teacher of physics in our colleges and universities with the view that progress in science depends on *his* knowledge of the domain in which he works, *his* scientific curiosity, *his* scientific imagination, *his* experimental skill and analytical ability, and that progress is likely to be accompanied by the scientific analogues of blood, sweat, and tears.

Technical Papers

The Similarity of the Effect of Podophyllin and Colchicine and Their Use in the Treatment of Condylomata Acuminata

MAJOR LESTER S. KING and
MAJOR MAURICE SULLIVAN[1]
Wm. Beaumont General Hospital, El Paso, Texas

The drug podophyllin, after having been dropped from the official list of cathartics in the *Pharmacopeia*, has become of renewed interest in dermatology. Kaplan (*1*) reported the use of podophyllin in oil as a topical application in the treatment of condylomata acuminata, with very satisfactory clinical results. Clinical trials have fully confirmed the efficacy of the drug. Its mode of action, however, has hitherto received no attention.

The application of podophyllin to normal human and rabbit skin reveals unusual changes affecting the epidermis. There is alteration of nuclear pattern, leading to the breakup of chromatin masses and the production of varying-sized pycnotic fragments. In other cells the disintegration of chromatin resembles markedly distorted mitotic figures, principally but not exclusively of the metaphase. There are corresponding cytoplasmic changes consisting, in different cells, of spongy swelling, shrinkage from the cell membrane, hydrops, delicate fibrillation, and alterations of standing reactions. We designate such altered cells as "podophyllin cells."

In many rabbits practically every cell in the epidermis discloses these severe nuclear and cytoplasmic alterations. The changes are transitory, and an essentially normal epidermis is re-established four to six days after a single application. Repeated applications show no increase in effect. On the contrary, a resistance seems to be established, and the histologic appearance following 20 applications is less striking than that following a single application. There is no evidence of cumulative effect in the experiments thus far undertaken.

Histologic examination of condylomata in the process of undergoing involution following applications of podophyllin shows numerous "podophyllin cells" of the type readily observed in the experimental material. In addition, there are widespread, nonspecific, degenerative changes in the epithelial cells.

The "podophyllin cells" were found to resemble the so-called "colchicine figures" described in the literature (*2, 3*). Consequently, suspensions of colchicine in oil were applied to condylomata acuminata, with clinical results superior to those of podophyllin. Similar colchicine suspensions applied to rabbit skin also resulted in pathologic alterations identical with the podophyllin effect, but more intense and of briefer duration.

Previously, in the experimental use of colchicine the drug has been injected parenterally, and its effect on various organs has been widespread. Its action has been considered to be to arrest mitosis in the metaphase. In the present work, colchicine and podophyllin, applied to the unbroken skin, do not suggest this mode of action. There is some direct, immediate, degenerative action, with resultant cell death. Other changes can be interpreted as a preliminary stimulation of mitosis, with marked distortion of the resulting pattern.

The differences between colchicine injected subcutaneously and colchicine applied locally can probably be attributed to the greater local concentration attainable with the latter method. It is of interest that podophyllin and colchicine are essentially without effect when applied to verrucae vulgares or other

[1] Present addresses, respectively: 836 Wellington Avenue, Chicago 14, Illinois, and 3301 North Charles, Baltimore 18, Maryland.

lesions with extensive keratinization. This suggests that the penetrating power of the drugs is slight.

It is known that totally unrelated compounds have actions similar to colchicine. Ludford (*3*) mentions auramine, urethane, and sodium cacodylate as producing the same effects as colchicine on injection. Podophyllin, by local application, is now shown to have the same results as colchicine.

Detailed descriptions of our clinical and pathological studies will be reported.

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X-Ray-induced Depolymerization of Thymonucleohistone and of Sodium Thymonucleate[1]

A. H. SPARROW and FLORENCE M. ROSENFELD
Biological Laboratories, Harvard University

It is well known that X-rays greatly increase mutation rates and produce chromosome breaks and aberrations, but the mechanism by which these effects are brought about is not well understood. It is assumed that excitations or ionizations produced by the X-ray quanta cause molecular disturbances or rearrangements which ultimately lead to visible chromonemal breaks or gene mutations (*2, 5*). Practically nothing is known about the very complex chain of events connecting the initial activation with the end result. It appeared that an investigation of the effects of X-rays on isolated chromosomal constituents might yield pertinent information. A study was therefore begun of the effects of X-rays on the physical properties of two important nuclear components: thymonucleohistone and the sodium salt of thymonucleic acid.

The nucleohistone used was prepared from calf thymus by the method of Mirsky and Pollister (*4*). Sodium thymonucleate was separated from the nucleohistone by saturation with sodium chloride as described by Bang (*1*) and Hammarsten (*3*). Both substances have characteristically high relative viscosities and show intense birefringence of flow. These properties serve as indexes of molecular asymmetry.

Solutions of 0.2 per cent sodium thymonucleate in water and 0.4 per cent thymonucleohistone in 1 M NaCl were irradiated. Viscosities were measured in the Ostwald type of capillary viscometer immersed in a water bath at 30 ± .05° C. Viscosities relative to the solvent for control (unrayed) samples and for rayed samples up to dosages of 120,000 r are given in Table 1. The data are presented graphically in Fig. 1.

TABLE 1
RELATIONSHIP OF X-RAY DOSAGE TO RELATIVE VISCOSITIES OF SOLUTIONS OF THYMONUCLEOHISTONE AND SODIUM THYMONUCLEATE

Dosage (r)	Relative viscosity	
	Nucleohistone	Sodium thymonucleate
0	3.47	3.97
7,500	3.27	3.50
15,000	3.10	3.13
30,000	2.72	2.26
45,000	2.54	1.99
60,000	2.21	1.61
90,000	1.79	1.25
120,000	1.74	1.15

Plotted on a semilogarithmic scale, these values give approximately straight-line curves for both nucleate and nucleohistone. However, the considerable differences in slope indicate that equal dosages cause a greater drop in viscosity of the nucleate than of the thymonucleohistone solution.

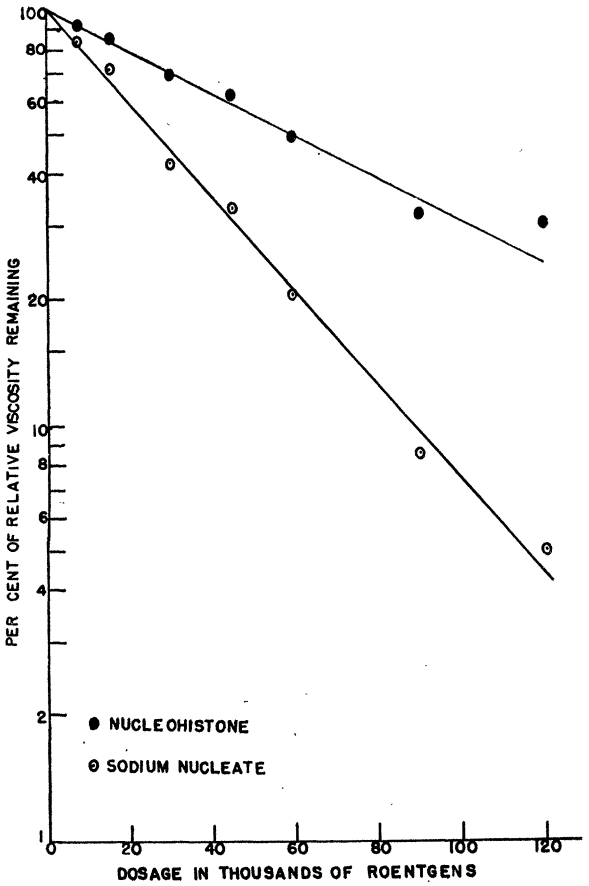

FIG. 1. Effect of X-ray dosage on relative viscosities of solutions of thymonucleohistone and sodium thymonucleate.

Streaming birefringence was present in both nucleate and nucleohistone solutions before raying. After

[1] This investigation was supported in part by a grant from the International Cancer Research Foundation.