

85 (902)

The action of radium on growing cells.By **F. C. WOOD** and **FREDERICK PRIME**.

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If it is difficult to correlate the published results of the clinical treatment of cancer with radium, it is still more difficult to correlate the findings in the biological study of radioactivity. My own experiments on primary mouse tumors, shortly to be published, show that it is impossible to cure primary carcinoma of mice by the application of 155 mgm. of radium bromide, even when used for long periods of time. Nevertheless, the tumors so treated shrink to a fraction of their previous size. Thus, after forty-eight hours' treatment of a tumor, about 15 mm. in diameter, with 30 mgm. of radium bromide, only a microscopic remnant could be found. von Wassermann¹ says, however, that the direct application of 55 mgm. of mesothorium for many days did not interfere with the growth of a transplanted mouse carcinoma, and yet he states that a small fragment of the same tumor irradiated for three hours with the same amount of mesothorium could not be successfully transplanted. Again, he says that carcinoma cells suspended in Ringer's solution have their "genoceptors" destroyed so that the cell cannot reproduce itself, though it is still alive and its nutrireceptors are active after three to three and a half hours. The method he uses to prove that the cells are still living is to suspend them in methylene blue solution; if this decolorizes, he considers that the cells are alive. The assumption is so questionable that it seems worth while to publish a few experiments out of a large series made in the Crocker Laboratory as a part of a general study of radium action.

Russell and Bullock² have recently taken issue with Von Wassermann and have drawn attention to some observations which contradict his statements, citing the experiments of Russ and

* George Crocker Special Research Fund.

¹ *Deutsch. med. Wchnschr.*, 1914, p. 524.

² *Berl. klin. Wchnschr.*, 1914, p. 725.

Wedd,¹ who discovered mitoses six days after the irradiated grafts had been implanted.

The preliminary experiments now to be reported do not wholly clear up these conflicting statements, and it is certain that a great deal more work must be done on a great variety of tissues with carefully measured quantities of radium and standard screening before we can obtain any insight into the effects exerted by this substance. We have noted, however, that 155 mgm. of radium bromide, screened with 1 mm. of aluminum and 0.18 mm. of coverglass, did not stop the beating of embryonal heart tissue in vitro, nor check a profuse outgrowth of connective tissue from the mass, after an exposure of three hours. So, too, the Flexner rat carcinoma, growing in rat plasma, when treated with 155 mgm. of radium bromide, screened with 0.4 mm. brass and 0.18 mm. coverglass, was not entirely inhibited in its growth by a three hours' exposure, though the amount of radiation was three times that used by von Wassermann.

In another series of the same tumor, however, growth was inhibited after an exposure of three hours to 155 mgm. of radium bromide, screened with 0.8 mm. of brass and 0.18 mm. of coverglass.

These absolutely contradictory results, representing a considerable series of experiments, show how cautiously we must draw conclusions as to the action of radium on cells when they are placed in unfavorable surroundings.

The growth of the Jensen rat sarcoma was inhibited, but not stopped, by an exposure of three hours to 30 mgm. of radium bromide, screened with 0.8 mm. of brass and 0.18 mm. of coverglass, while an exposure of three hours to 155 mgm. with the same filter stopped all growth. In this case, apparently, the sarcoma was more susceptible to radium than the carcinoma, while embryonal tissue was the most resistant of all. Similar differences were noted by Menten in radiating transplanted tumors. The same tumor tissue in vivo when exposed to radiation of far greater intensity is uninjured, as shown by its transplantability.

In conclusion, then, 155 mgm. of radium bromide, screened with 1 mm. of aluminum or 0.8 mm. of brass and only about 1.5

¹ *Arch. Middlesex Hospital*, 1912, XXVII, 50; see also Russ and Chambers, *ibid.*, 1913, XXX, 120.

mm. distant from beating embryonal heart tissue, does not kill it in three hours, and does not stop the growth of connective tissue cells. The same exposure, however, does prevent the growth of Jensen rat sarcoma, and inhibits but does not wholly prevent the growth of the Flexner rat carcinoma. Observations such as these show the danger of generalizing too freely from a limited number of experiments.

86 (903)

Note on the effect of animal extracts upon the secretion of the pancreas.

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Our experiments were made upon etherized cats who were killed before regaining consciousness. A Bernard cannula was inserted into the pancreatic duct inside the lumen of the intestine. The biliary duct was previously ligated. We then injected secretin solution into the jugular, as no secretion was noted before its injection. We then counted, after the injection of secretin, the number of drops falling every 5 minutes for three periods. Then we injected the same amount of secretin plus a watery solution of one of the dried glands. Then we counted for three periods the number of drops every 5 minutes. Finally we again injected the same amount of secretin solution and again noted the number of drops every 5 minutes for three periods. If in the second period we obtained a marked increase over or decrease below the first period and third period, we inferred that the animal extract had some action. We obtained the following results. We also have inserted their effects upon the volume of the gland for comparison.

Animal Extracts.	Pancreatic Volume.	Pancreatic Secretion.
Parathyroid	increases	increases
Secretin	increases	increases
Mammary	increases	increases
Infundibulin	decreases for 3 minutes then increases	decreases (Pemberton & Sweet)
Adrenalin	decreases for 3½ minutes then increases	decreases (Pemberton & Sweet)
Pinea	increases	increases