stand for a day before planting. Immersing the seeds in 3 and 6 per cent. solutions of ethylene chlorhydrin (made by mixing 6 and 12 milliliters, respectively, of ethylene chlorhydrin, technical, with 194 and 188 milliliters of water) also was effective. The seeds were immersed for a minute, the solution poured off of them and the bottle stoppered for twenty-four hours before planting.

With black and red oak acorns consistently good results have been obtained by subjecting 50 or 100 acorns in a liter wide-mouth bottle to the vapors of four milliliters of ethylene chlorhydrin, technical, for twenty-four hours. The chemical was placed on a five-inch square of cheesecloth suspended from the stopper. This treatment initiated germination of acorns gathered in October within four weeks and within ten weeks more than 70 per cent. had germinated while the acorns not treated showed 1 per cent. or no germination. Immersion of these acorns in a 3 per cent. solution of thiourea for 15 minutes was effective but slower than the ethylene chlorhydrin vapor treatment. Germination in acorns treated with thiourea solution did not start until the seventh to tenth week after treatment.

It is not claimed that the procedures described are the best methods of hastening dormant tree seeds into germination with chemicals since much more work needs to be done upon the most effective concentrations of the chemicals and the most effective time periods of treatment but these chemicals do give a new mode of attack upon dormancy in seeds. The results reported are based on tests made with more than 9,000 maple seeds and 5,000 acorns.

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SPECIAL ARTICLES

THE BIOLOGICAL EFFECT OF HIGH VOLTAGE X-RAYS

FOR many years radiologists have debated the question whether equal doses of X-rays of different wave-lengths produce the same or different quantitative biological effects, a problem of practical importance in therapy. The chief obstacles in deciding the matter were the lack of a standard unit of X-ray intensity, the lack of adequate measuring apparatus and the highly variable character of the biological materials which were used in making the tests. The adoption of a standard unit, the Roentgen, now permits an accurate definition of dosage, where previously none was possible. The question now is this: When a definite number of r units, measured by an air ionization chamber, is delivered to a suitable material, will the amount of effect which is produced vary with the wave-length of the beam, that is, with the voltage.

An almost ideal biological material consists of the eggs of the wild fruit fly, Drosophila. These eggs when freshly laid are comparatively sensitive, and are remarkably uniform in response. Different strains of wild flies are apparently equally radiosensitive. Therefore one may make experiments with them anywhere with the assurance that his results will be comparable with those obtained by other workers at other places.

A long series of tests[1] with carefully measured beams produced at constant potentials shows that the mortality curve has an asymmetrical sigmoid shape. These tests were made with different wave-lengths, (0.20, 0.50 and 0.70 A. U.), that is, with hard, medium and soft X-rays. In each instance the results showed that the quality of the beam has no effect on the mortality rate; it is the intensity which is the deciding factor. Furthermore, the course of the curve is the same in each case. From such a curve we can determine how many r units are required to kill any percentage of eggs in a sample.

The method may be reversed.[2] By knowing how long a dose is needed to kill, say 50 per cent. of the eggs, we can estimate the intensity with considerable accuracy. Half the eggs are killed by 180 r units. If 10 minutes are required to kill this proportion, the intensity was 18 r/min.

The wave-lengths employed lay within the range of ordinary radiotherapeutic practice, that is, they were produced at potentials of 50 to 180 KV. But now that machines capable of running at much higher voltages are being developed it is necessary to determine whether a definite dose of these very short waves is biologically equivalent to an equal dose of longer waves. We have recently made this test at the California Institute of Technology where a tube which operates at 550 KV is in use.[3]

In these experiments the X-rays were filtered through 6 mm of steel, the emergent beam having an effective wave-length of 0.04 A. U. Ionization tests showed that at the point where the eggs were exposed the intensity was 15 r/min. This includes a small amount of scatter from the walls of the room, amounting to perhaps 1 r/min. The eggs were given 120, 180 and 240 units. From the curve we should expect the percentages of eggs killed to be 22, 50 and 67 per cent. The actual results, which are averages of many tests

[1] Packard, C., *J. Cancer Res.*, 1927, 11, 1.

[2] Packard, C., *J. Cancer Res.*, 1927, 11, 282.

[3] Lauritsen, C. C. and B. Cassen, *Phys. Rev.*, 1930, 36, 988.

involving some thousands of eggs, were 23, 49.5 and 68.5 per cent. Obviously then the fly eggs react to doses of these very short waves in precisely the same way as they do to softer radiation. A further test at 300 KV (0.07 A. U.) demonstrates the same fact.

Another experiment with a different biological material gave similar results. A mouse tumor (Sarcoma 180) was cut into small pieces which were radiated and then inoculated into healthy animals. The criterion of effect was the failure of the radiated pieces to grow. Untreated particles always "take." A number of tests at 550 KV showed that the lethal dose was about 2750 r. This is the same as that found by Wood[4] who used much softer rays (0.20 and 0.70 A. U.).

The conclusion is that between 0.04 and 0.70 A. U. the biological effect of equal doses is the same. How far this equality extends in the direction of still shorter waves, *e.g.*, the gamma rays of radium, and of very long waves produced at a few thousand volts, is still to be determined. Since the effect is produced by secondary radiations generated when the primary radiation is absorbed, it may be expected that there will be an equality through a much wider range of wave-lengths than have thus far been used. Experiments on the action of the Grenz rays whose wave-lengths are from 1.0 to 2.0 A. U. are now in progress.

Because of the great penetrating power of the high voltage rays it is possible to deliver to deep lying tissue a much larger proportion of the incident energy than is possible with less penetrating rays. Theoretically this should be of value in therapy; whether such rays will prove advantageous in practice can be determined only by careful study of the reaction of the patients.

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THE CORTICO-ADRENAL HORMONE

AN outstanding advance in the physiology of the internal secretions has been made by the development in the past year of potent aqueous extracts of the adrenal cortex. Nearly simultaneous announcements of the maintenance of adrenalectomized animals in perfect health by the administration of cortico-adrenal extracts has been made by Hartman and his collaborators at Buffalo,[1] and by Swingle and Pfiffner at Princeton.[2] The latter observers kept several of their cats alive and in good health over 100 days; Hartman reports that three of his animals lived over 100 days, and one over 200 days. The insignificant effect of cortico-adrenal extracts which have been developed by previous workers has been dealt with at length in a recent review.[3]

In this laboratory we have recently made and tested cortico-adrenal extracts prepared according to the methods of both the Buffalo and the Princeton investigators. The method of Swingle and Pfiffner, although long-drawn-out (taking usually 10 to 14 days) and offering many possibilities for the loss of potency to occur, is simple to carry out; that of Hartman takes only a few days but offers technical difficulties, particularly in the elimination of inert lipoid substances and of adrenalin. On adrenalectomized cats we have tested to date eighteen batches of extract made according to the Swingle-Pfiffner technique, and six batches prepared after Hartman's method.

It can be said positively that the Swingle-Pfiffner extracts contain significant amounts of the cortico-adrenal hormone. On administration of the substance to adrenalectomized cats the life span is at least much prolonged, and may possibly be extended indefinitely. The animals gain in weight and look apparently normal. We have given particular attention, however, to the recovery of animals from the severe symptoms of adrenal insufficiency, and have therefore stopped administration of the extract three or four weeks after adrenal removal, and often earlier. Evidences of resuscitation of adrenalectomized cats from extreme prostration following intraperitoneal injection of the Swingle-Pfiffner extract are apparent in 15 to 30 minutes: convulsions are suppressed, the animals show an interest in their surroundings and attempt to sit up; within an hour or so they may walk about and appear practically normal, and two hours after injection they may take food. Examples of recovery are given from a few of our protocols in Table 1.

We have made up the extract to a final concentration of 30 grams of cortex per cubic centimeter—or 100 cubic centimeters of extract per 4 kilos of fresh ox glands. The injections have chiefly been given intraperitoneally. Usually it has been necessary to inject from 5 to 10 cc of extract per kilo body weight of the animal, in the course of 24 hours, to effect restoration from the pronounced symptoms of adrenal insufficiency. Twenty cc of the extract given intraperitoneally to a small (two-kilo) cat have produced no ill effects. The material is also non-toxic when given subcutaneously, intramuscularly, intravenously or intracardially. In one case injection by the latter route was strikingly effective in resuscitating a coma-

[4] Wood, F. C., *Radiology*, 1925, 5, 199.

[1] F. A. Hartman, K. A. Brownell and W. E. Hartman, *Amer. J. Physiol.*, 95: 670, 1930.

[2] W. W. Swingle and J. J. Pfiffner, *Amer. J. Physiol.*, 96: 153, 1931.

[3] S. W. Britton, *Physiol. Reviews*, 10: 617, 1930.