level remained about three times greater than that of the controls for several days after the cessation of zirconium therapy.

A small part of the heightened excretion was due to the sodium citrate solvent. However, the amount of plutonium eliminated by the animals treated with sodium citrate alone fell abruptly to pretreatment levels after the sodium citrate injections were discontinued.

None of the treatments significantly altered the quantity of plutonium excreted in the feces.

Tissue analyses revealed that the zirconium-treated rats had only about half as much plutonium in the skeleton and in the liver as the control animals, but the concentration of plutonium in the muscle and kidneys of these animals was greater than that found in the controls. The bone and liver concentrations of plutonium in the rats treated with sodium citrate did not seem to differ appreciably from those in the controls.

Five months after the dog received an intravenous injection of 0.058 mg. of plutonium/kg. treatment with very small doses of zirconium citrate (4–16 mg./kg. of body weight), injected intravenously, was begun. A very definite increase in urinary excretion of plutonium occurred within the first few days following each dose of zirconium. The extent of the rise in the elimination rate in the urine was directly proportional to the amount of zirconium injected. The increased rate of excretion was continued for at least three weeks after the cessation of zirconium treatment. Even with these dosage levels, which were far below the maximal dose by a factor of at least 10, the elimination rate of urinary plutonium was increased more than 150 per cent over the pretreatment level.

The average excretion of plutonium in the feces of the dog, following the zirconium treatment, appeared to increase but slightly.

In rats treated with zirconium about five weeks after the injection of plutonium, a roughly 10-fold increase in the urinary excretion of plutonium was observed. These animals were sacrificed shortly after treatment and were found to have only half as much plutonium in the liver as the controls. The bone content of plutonium was unchanged.

It appears, therefore, that zirconium first acts to displace plutonium from the liver. Later it migrates to the bone and slowly but continuously displaces the deposited plutonium to an extent which depends on the concentration of zirconium relative to the plutonium.

Radioautograph studies (*1*) have shown that plutonium, cerium, yttrium, and zirconium are laid down in the uncalcified organic matrix of the bone and in the endosteum and periosteum. Strontium, on the other hand, is deposited almost exclusively in bone salt, and it might be expected that zirconium treatment would have little effect in cases of radiostrontium poisoning. This was shown experimentally where it was found that zirconium treatment had only a negligible effect on the excretion rate of radiostrontium and on its concentration in the liver and bone of rats. Experiments to test the effect of zirconium treatment in cases of radioyttrium poisoning are in progress.

A study of the toxicity of zirconium and other metals revealed that zirconium was by far the safest for therapeutic use. When zirconium was given in single massive doses of 1.5, 1.75, and 2.0 grams/kg. of body weight, the percentages surviving were 100, 50, and 0, respectively. No harmful chronic effects have as yet been found.

Within 24 hours after the injection of zirconium, 80–90 per cent of the metal was excreted in the urine. Its fecal excretion is, however, very low.

The action of sodium citrate in promoting the excretion of plutonium can be attributed to its ability to increase the diffusibility of plutonium (*2*) and thus facilitate its clearance through the kidney.

Further investigations of metal displacement therapy in cases of chronic poisoning by plutonium and other long-lived radioelements are in progress.

References

1. Copp, D. H., Axelrod, D. J., and Hamilton, J. G. The deposition of radioactive metals in bone as a potential health hazard. (To be published.)
2. Schubert, J. Unpublished work completed in June 1946.

Effect of Temperature on the Growth and Sterility of Maize

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Varieties of corn grown in the Northeast and in the Middlewest at the same latitude are noticeably taller in the East. Several environmental conditions, principally light intensity and temperature, are involved in this growth difference. Plants of many species, including maize, grown under tobacco shade cloth are significantly taller and broader in leaf than plants from the same lot of seed grown in full sunlight. Under the cloth shade the temperature is the same as outside, but the humidity is higher and the light intensity is lower. The same effect is noticed in the field, where short-stalked varieties of corn are grown in single rows between taller varieties. Where there is a wide alley between ranges, the plants at the ends of the rows are shorter than those in the center of the rows, the plants graduating in height. Here humidity and temperature are the same, but light intensity varies.

Some corn seedlings started in the greenhouse and set outdoors were shorter at maturity than plants from the same seed started outdoors. This indicated that temperature in the early stages of growth had an effect. To test this, seeds of a uniform, vigorous, first-generation hybrid ($WF_9 \times$ P8) were germinated in an incubator at about 30° C. until the shoots and roots were from $\frac{1}{4}$ to $\frac{1}{2}$ inch long. Three different lots of these sprouted seedlings were held at 40, 50, and 60° C. for one hour, after which they were planted in pots and left in the greenhouse until it was certain the plants would grow. They were then set in the field alongside plants from the same lot of seed sown in the open ground at the same time the treated seedlings were started in the incubator. Some of the heat-treated seedlings died, but enough were started in each lot and later thinned to give an even stand of plants in the field.

All three lots of heat-treated seedlings were shorter in height, less vigorous in growth throughout the season, and later in flowering than the untreated plants. All lots grew to full maturity and were measured after growth had ceased. The results in inches of height were: control, 101; 40° C., 87; 50° C., 89; and 60° C., 93, *i.e.* an average of 90 inches in

height for the heat-treated lots compared to 101 inches for the control.

An unanticipated result was the pollen sterility in all treated lots. Normal tassels were produced with well-developed florets, but the anthers were small and shriveled and for the most part remained enclosed in the glumes. In view of the fact that high temperatures sterilize the male germ cells in animals from amphibians to mammals, these results are highly significant. This influence on growth is an antivernalization effect and may have wide usefulness in the production of hybrid seed, especially if it is shown by plants other than maize. Further experiments are in progress.

Failure of Sodium Salicylate to Inhibit Hyaluronidase *in Vitro*

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When India ink or Evans Blue was injected with hyaluronidase into the skin of rabbits or human subjects following the administration of sodium salicylate, Guerra (*1*) observed decreased spreading as compared with normal controls. If this result was due to the inhibition of hyaluronidase by sodium salicylate, as concluded by Guerra, it should be possible to demonstrate an antagonistic effect of sodium salicylate on hyaluronidase *in vitro*.

Using the broth culture filtrate of a mucoid group A streptococcus as substrate, it was found that 0.005 ml. of a crude bovine testicular extract completely destroyed 0.5 mg. of hyaluronic acid. The addition to the reacting mixture of 5 mg. of sodium salicylate did not decrease the rate of disappearance of the hyaluronic acid, the amount of which was estimated by precipitation with acidified dilute horse serum (*3*).

In a second experiment, 1:100 dilution of crude testicular extract was prepared in 10 per cent sodium salicylate. This solution, as well as a 1:100 dilution of the same testicular extract without sodium salicylate, was tested for its ability to prevent the mucin clot formation by potassium hyaluronate prepared from human umbilical cord (*2*). Both solutions prevented clot formation, again indicating no inhibition of testicular hyaluronidase by the sodium salicylate.

The action of sodium salicylate on streptococcal hyaluronidase was also examined. A broth culture filtrate of a nonmucoid group A streptococcus as a source of the enzyme was combined with a filtrate of a mucoid group A streptococcus containing hyaluronic acid. The enzyme destroyed 0.5 mg. of hyaluronic acid on incubation overnight. The inclusion of 0.1 per cent sodium salicylate in the system did not alter the reaction. When broth containing 10 mg. per cent of hyaluronic acid was inoculated with a nonmucoid group A streptococcus, the hyaluronic acid was destroyed by the time maximum growth was attained. The addition of sodium salicylate to the broth did not retard the disappearance of the hyaluronic acid except in concentrations that inhibited growth. Sodium salicylate, 0.1 per cent, was slightly bacteriostatic; 0.05 per cent inhibited neither growth nor the destruction of the hyaluronic acid.

These experiments fail to demonstrate any inhibitory effect of sodium salicylate on testicular or streptococcal hyaluronidase.

References

1. GUERRA, F. *Science*, 1946, **103**, 686; *J. Pharm. exp. Therap.*, 1946, **87**, 193.
2. MCCLEAN, D. *Biochem. J.*, 1937, **43**, 169.
3. SEASTONE, C. V. *J. exp. Med.*, 1939, **70**, 361.

The Carcinogenic Action of Smegma[1]

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Carcinoma of penis does not occur in people who have been circumcised in the first weeks of life and is rare in people who have been circumcised in childhood or in early puberty. Circumcision in adult life does not affect the frequency of the disease. Phimosis seems to be a predisposing factor. Penile cancer is frequent where personal hygiene is poor; it is rarer where bathrooms are plentiful. All this has been known for decades, and various opinions have been expressed concerning causal relations. Little has been done, however, to establish experimentally the possible carcinogenic action of smegma. Fishman, Shear, Friedman, and Stewart (*1*) injected filtered suspensions of human smegma subcutaneously into 12 young mice of the A strain. No tumors were obtained either in these mice or in 20 young mice into whose distended vaginas smegma was introduced.

In our experiments mice of the Paris R 3 strain were used. No spontaneous malignant tumors of skin and no cutaneous papillomata have been observed in many thousands of mice of this strain in the Crocker Cancer Research Institute. Some of the mice were bred in the Crocker Institute, others in Beth Israel Hospital. They were kept in wooden cages with wire covers, were fed Rockland pellets, and were given water.

Since human smegma, which was used in the first experiments, could not be obtained in sufficient amounts, horse smegma was substituted. This particular substitution was made because penile cancer is frequent in the horse. Smegma is best obtained from dead horses in rendering plants or from anesthesized animals in a department of veterinary surgery. The smegma was kept dry in glass jars in the refrigerator or at room temperature. Generally it was impossible to discover whether the material came from a stallion or from a gelding. One batch was examined for male and female sex hormones, but none were found.

The nonsaponifiable fraction was prepared in the usual way. An analysis for fatty substances gave the following result: total fat, 45 per cent of dry substance (fatty acids, 32.2 per cent; phosphatids, 3.9 per cent; total cholesterol, 6 per cent; cholesterol esters, 2 per cent).

Cerumen, which resembles smegma in being a skin product that is retained on or near the surface of the body, was used

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