Whether or not this hypothesis holds true, we believe that our data on sodium citrate protection against uranium injury point to the maintenance of one or more vital equilibria (possibly the "citric acid cycle" of carbohydrate metabolism[6]) while the normal processes of repair are taking place, for we have no evidence that repair is accelerated or altered in any way.

Summary. Nineteen of 20 adult dogs survived a lethal dose of uranium nitrate (5.0 mg/kg) when large doses of sodium citrate (0.23 g/kg/day for 5-10 days) were injected intravenously. The citrate injections were as effective when started as late as 67 hours after the heavy metal as when started immediately after the injection of uranium nitrate.

Objections are raised to the currently accepted view that maintenance of the alkali reserve is the mechanism whereby protection is afforded, and the suggestion is offered that sodium citrate supplies ions or molecules that keep the vital "citric acid cycle" of carbohydrate metabolism going while recovery takes place.

[6] Krebs, H. A., and Johnson, W. A., *Biochem. J.*, 1937, **31**, 645.

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Maternal Inheritance of Protoporphyrins of the Harderian Glands in Mice.

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Data indicating a parallelism between the amount of protoporphyrins in the Harderian glands of mice and intrinsic susceptibility to cancer of the mammary gland have been published.[1,2] Mice belonging to inbred strains with a high incidence of spontaneous mammary tumors have a very high concentration of protoporphyrins (deep red fluorescence under ultraviolet light); mice of strains with intermediate degrees of tumor susceptibility show an intermediate "pink" fluorescence; and mice of cancer-resistant strains exhibit very little or none of the fluorescence characteristic of protoporphyrins. Moreover, female mice of a cancer-susceptible strain (C_3H) have a higher concentration of protoporphyrins in their Harderian glands than males of the same strain and age.[3] *Only* female mice of a cancer-susceptible strain develop breast cancer spontaneously.

The problem of immediate interest is, can further studies on the determination of protoporphyrin concentration throw additional light (or reveal further parallelisms) on their level and the phenomena of susceptibility and resistance to spontaneous cancer? Among the most interesting (and perhaps the most important) observations in the analysis of the genetic influence on cancer susceptibility and resistance in mice is the finding that susceptibility to cancer of the breast in the F_1 individual is determined by the female parent (maternal inheritance).[4]

Chart I presents the data obtained on the red fluorescence (hence protoporphyrin concentration) in mice of the (a) C_3H strain (high or maximal protoporphyrin in the Harderian gland and high cancer susceptibility), (b) JK strain (minimal or low protoporphyrin and low cancer susceptibility), and (c) the 2 F_1 classes obtained by crossing mice of the parental stocks in both directions. The first F_1 generation was obtained by crossing a

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[1] Strong, L. C., and Figge, F. H. J., *Science*, 1941, **94**, 331.

[2] Figge, F. H. J., Strong, L. C., Strong, L. C., Jr., and Shanbrom, A., *Cancer Research*, 1942, **2**, 335.

[3] Strong, L. C., PROC. SOC. EXP. BIOL. AND MED., 1942, **50**, 123.

[4] Little, C. C., and Staff Roscoe B. Jackson Memorial Laboratory, *Science*, 1933, **78**, 465.

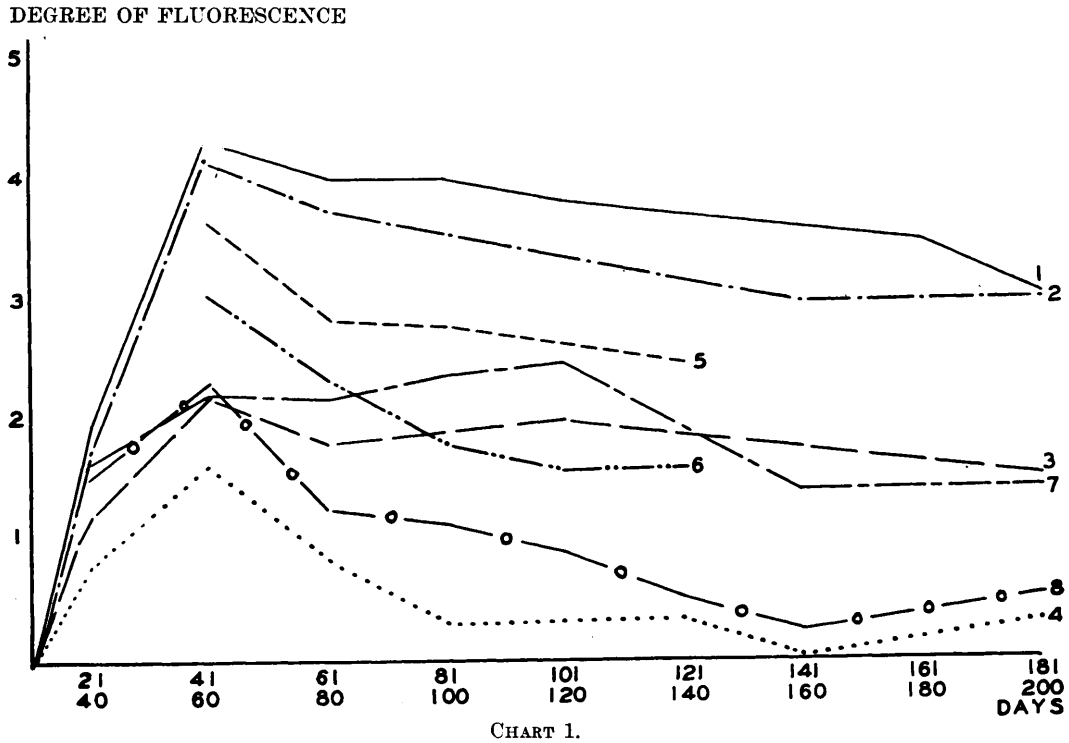

CHART 1.

This chart presents the data on the degree of red fluorescence under ultra-violet light (presence of protoporphyrins of the Harderian glands of mice). The reading of fluorescence is given on the vertical line; the age of the mice along the base line. Data on the C_3H are given on curves (1) female, and (2) males. Data for the JK mice on curves (3) female and (4) males. Data on F_1 (C_3H females $\times$ JK males) on curves (5) female, and (6) male. Similar data on F_1 (JK females $\times$ C_3H males) on curves (7) female and (8) male.

female of the C_3H strain with a male of the JK strain, and the second F_1 generation obtained by crossing a JK female with a C_3H strain male. Data obtained on the two sexes are presented separately. 1826 mice were used in this experiment—the data being divided into the various points (age) indicated in Chart I. At least 5 mice were used at each age point, thus producing a reliable curve for each of the groups.

An inspection of the chart will disclose the following facts: (a) in all classes the degree of red fluorescence rose rapidly, beginning as soon as the eyes were open and continuing through adolescence and into early sexual maturity, and then gradually declined, with advancing age, at approximately the same rate, in all cases. The main difference between the groups was the height attained by the red fluorescence before the decline set in; (b) in all cases the reading for the female was higher (approximately 25% higher, consistent with previous chemical extraction studies) than for the males of the same strains and classes;[3] (c) the reading for the F_1 generation was between the corresponding reading of the two ancestral stocks; and (d) the reading of the F_1 generation was closer to the reading for the female ancestral stock than for the male stock (maternal inheritance).

Conclusion. Thus the conclusion seems justified that another parallelism between cancer susceptibility and the presence of protoporphyrin in the Harderian gland is evident (maternal inheritance). Such a series of observations (even though they be in the nature of parallelism or correlation only) seems to be more than fortuitous. The level of protoporphyrins in the Harderian gland is probably a reflection of protoporphyrin metabolism throughout the body, and whether protoporphyrins (probably by a sensitizing action) have any effect on cancer or not must be tested further by the suitable administration of protoporphyrins to experimental animals. This experiment is in progress.