

than in the older ones (Group IV), the mean tumor age being in Group II 10.7 months, and in Group IV 17 months. Three months of this interval can be accounted for by the 3 months' delay of the hormonal treatment in the older group. However, the additional 3.3 months' difference has to be attributed to conditions of the experiment. Although the absolute number of tumors observed in these two age groups is small, the increase in the latent periods is in agreement with the decrease in the tumor incidence. It is, therefore, not unlikely that both are governed by

similar factors.

Summary. Male mice of strain C3H castrated at the age of 3 to 4 weeks and injected with alpha estradiol benzoate immediately after castration develop a larger number of breast cancers than males castrated at the same age but injected from the age of 4 months on. Thus, an age factor operates in the susceptibility to estrogen-induced mammary cancers in male mice. This age factor is independent of the testicle but acts synergistically with it.

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Effect of Insulin and Glucose Upon Survival Time of Eviscerated Rats.

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The data of these experiments show that the administration of glucose with insulin to the eviscerated rat permits longer survival times than the administration of glucose alone.

Methods. Male rats of the Sprague-Dawley strain were fed Friskies Dog Cubes. At a weight of 185 to 205 g, the inferior vena cava was ligated between the liver and the kidneys in order to cause the development of a collateral circulation. Asepsis was preserved in this operation. When the animals reached a weight of 250 ± 2 g they were anesthetized (intraperitoneal injection of 18 mg of cyclopentenylallyl-barbituric acid sodium) and eviscerated by the method of Ingle and Griffith.¹ Hemostasis was attained by applying a gelatin sponge (Gelfoam, Upjohn) with thrombin to the stumps of the oesophagus, colon, ligated vessels and between the muscle and the skin when the incisions were closed. The animals were not fasted prior to operation. Intravenous infusions of solutions of glucose (C.P. Dextrose, Merck) in 0.9% saline with and without added insulin (Crystalline zinc in-

sulin, Lilly) were made by continuous injection machines which delivered fluid into the saphenous vein of the right hind leg at the rate of 20 cc per 24 hours. The glucose loads used in this experiment represent amounts which sustain the average level of blood glucose at approximately normal values during a period of 24 hours. Temperature was constant at $26.5 \pm 0.5^\circ\text{C}$.

The time at which the heart of the rat stopped beating was determined by use of a heart-beat amplifier (Model A, Upjohn) which was designed to amplify the D.C. potential generated by the heart beat to actuate a 6-point recording mechanism (Leeds and Northrop Micromax S.) This apparatus gives a permanent visual record of an all-or-none response of the amplifier to the beating heart for 6 animals simultaneously.

In Experiment 1, 21 eviscerated rats were given a glucose load of 4 mg per 100 g of rat per hour (4/100/h). The average survival was 1748 minutes $\pm$ 113 (standard deviation of the average). Glucose loads of 4/100/h without insulin and 40/100/h with insulin are each able to sustain approximately normal levels of blood glucose during 24 hours

¹ Ingle, D. J., and Griffith, J. Q., Chapter 16, *The rat in laboratory investigation*. J. B. Lippincott Co., Philadelphia, 1942.

and longer. Twenty-two similar rats were given a glucose load of 40/100/h with 4 units of insulin per 24 hours per rat. The average survival was 2017 ± 77 minutes. The standard deviation of the difference (269) between the averages was 137 giving a ratio of 1.96 between the difference and its standard deviation, thereby indicating a statistical probability of 95 chances in 100 that the average survival of insulin treated rats is greater than the average survival of rats not treated with insulin.

In Experiment 2, 20 eviscerated rats were given a glucose load of 6/100/h without insulin. The average survival was 1828 ± 114 minutes. Twenty-one eviscerated rats were given a glucose load of 44/100/h with 4 units of insulin per 24 hours per rat. The average survival was 2194 ± 75 minutes. The standard deviation of the difference (366) between the averages was 137 giving a ratio of 2.7 between the difference and its standard deviation, thereby indicating a statistical probability of 99 chances in 100 that the average survival of the insulin treated rats was greater than the average survival of the rats not treated with insulin.

When the survival times for the insulin

series of both experiments were averaged together and the survival times for the no-insulin rats were averaged together, the standard deviation of the difference (316) in averages was 54 giving a ratio of 5.85 between the difference and its standard deviation, thereby indicating that the direction of the difference in averages was highly significant from the standpoint of statistical probability.

Discussion. This is one of a series of studies on factors which influence the survival of eviscerated rats. The times of survival can be prolonged by the continuous intravenous injection of saline only;² the addition of glucose without insulin prolongs survival and the administration of higher loads of glucose with insulin gives further prolongation of average survival times. The longest survival of any animal in these experiments was 44 hours and 4 minutes.

Summary. Eviscerated rats were given continuous intravenous infusions of glucose in saline. The addition of insulin and glucose prolonged the survivals of these animals to a greater extent than did glucose without insulin.

² Ingic, D. J., Sheppard, R., and Winter, H. A., *Am. J. Physiol.*, 1945, **144**, 255.

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Effect of Diethyldithiocarbamate on the Respiration of Active and Blocked Embryonic Cells.*

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The action of urethanes (carbamates) on respiration and related phenomena of living cells, in general, shows a marked stimulation with low doses and a corresponding definite inhibition with higher concentrations.¹ The

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¹ Fisher, K. C., and Henry, R. J., *J. Gen. Physiol.*, 1943, **27**, 469.

efficiency of homologous series of these compounds in producing these reactions increases markedly with their increase in carbon content.² Recent results concerning their carcinogenic activity add further interest to an elucidation of their basic reactions upon living cells and tissues.³ The present report is concerned with results of experiments upon

² Taylor, G. W., *J. Cell. and Comp. Physiol.*, 1936, **7**, 409.

³ Larsen, C. D., *J. Nat. Cancer Inst.*, 1947, **8**, 99.