Im folgenden wird über die erfolgreiche heterologe Transplantation eines Mäusetumors auf junge Ratten, die mit radioaktiven Isotopen vorbehandelt wurden, berichtet[1].

Methodik. Wir verwendeten das Crocker-Sarkom der Maus, das wir in Form von etwa 1 mm³ grossen Stücken auf junge Albinoratten von 50 g Gewicht subkutan transplantierten. Als Mass der Tumorgrösse diente uns das Produkt aus den beiden grössten Durchmessern des Tumors.

P^{32} wurde als Lösung von $Na_2 HPO_4$ intraperitoneal injiziert. Au^{198} wurde als kolloidales Präparat teils intravenös, teils intraperitoneal appliziert. 16 Ratten erhielten je 0,125 mC P^{32} in 0,25 cm³ Lösung intraperitonäal injiziert. Je 8 Ratten wurden am 1. bzw. 11. Tag nach der P^{32}-Injektion mit dem Crocker-Sarkom der Maus implantiert. 16 Ratten wurde eine Injektion von je 0,75 mC Au^{198} in 0,23 cm³ Lösung intravenös und weiteren 16 Ratten dieselbe Dosis intraperitoneal verabreicht. Bei je 8 Ratten aus beiden Versuchsgruppen wurde die Heterotransplantation 1 bzw. 5 Tage nach der Injektion durchgeführt.

Resultate. Die Resultate dieser Experimente sind aus der Tabelle ersichtlich.

Mittelwerte der maximalen Tumorgrösse von je 8 auf gleiche Weise behandelten Ratten.

Vorbehandlung	Maximum der Tumorgrösse in mm² (Länge × Breite)
Kontrollen	51
P^{32} *i.p.* Heterotransplantation:	
1 Tag nach Injektion	142
11 Tage nach Injektion	253
Au^{198} i.p. Heterotransplantation:	
1 Tag nach Injektion	88
5 Tage nach Injektion	256
Au^{198} i.v. Heterotransplantation:	
1 Tag nach Injektion	109
5 Tage nach Injektion	150

Das Maximum der Tumorgrösse wurde bei allen behandelten Tieren zwischen dem 8. und 12. Tag nach der Transplantation erreicht. Bei allen mit radioaktiven Isotopen vorbehandelten Ratten wächst der Maustumor stärker als bei den Kontrollen. Bei grösserem Intervall zwischen Injektion von P^{32} oder Au^{198} und der Heterotransplantation entwickelt sich der Tumor besser als bei kurzem Intervall. Nach intraperitonealer Goldinjektion entwickelt sich der heterolog transplantierte Tumor (bei fünftägigem Abstand zwischen Injektion und Implantation) besser als nach intravenöser Goldapplikation. Die Resultate zeigen, dass bei Behandlung der Wirtstiere mit recht verschiedenen Strahlungsarten die Heterotransplantation ermöglicht wird. P^{32} ist ein reiner β-Strahler, während Au^{198} ein gemischter β-γ-Strahler ist. Ferner kann bei verschiedenster Verbreitung und Lokalisation der radioaktiven Isotope im Wirtsorganismus die Entwicklung des heterologen Tumors erfolgen. P^{32} wird besonders von Knochen, Knochenmark, Lymphdrüsen, Leber, Milz, Niere und in geringem Masse von den meisten Geweben des Körpers aufgenommen. Kolloidales Au^{198} wird bei intravenöser Applikation fast ausschliesslich vom retikuloendothelialen System gespeichert. Bei intraperitonealer Verabreichung bleibt Au^{198} weitgehend in der Peritonealhöhle liegen[1]. Die unterschiedliche Wachstumstendenz der Tumoren nach Vorbehandlung der Wirtstiere mit verschiedenen radioaktiven Isotopen, bei verschiedener Applikation und bei verschieden langem Intervall zwischen Injektion und Heterotransplantation erklärt sich wahrscheinlich durch die verschiedenartige Hemmung der Abwehrkräfte des Wirtsorganismus gegen den heterologen Tumor.

W. BOLLAG und CL. MEYER

Medizinische Universitätsklinik Zürich, den 25. Januar 1954.

Summary

The investigation deals with the successful heterologous transplantation of the Mouse Crocker-Sarcoma on young rats, that were pretreated with the radioactive isotopes P^{32} and Au^{198}. The growth tendency of the tumours varies according to the character of the radioactive isotope, the mode of administration and the interval between the injection of the radioactive substance and the heterotransplantation.

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Sulfhydryl Groups and Succinic Dehydrogenase in Rat Kidney after Administration of Mercurial Diuretics

Histochemical Studies

Recently we reported[1] that, when blue tetrazolium (BT) is used as a histochemical indicator, the administration of mercurial diuretics to rats inhibits the succinic dehydrogenase activity in kidney cells, particularly in the cells of HENLE's loops. By biochemical means, HANDLEY and LAVIK[2] previously demonstrated a fall in the total succinic dehydrogenase activity in rat kidney after administration of mercurials.

Sulfhydryl groups are essential for the normal activity of succinic dehydrogenase. That the diuretic effect of mercurials, which combine with sulfhydryl groups, is attributable to the sulfhydryl-requiring enzymes seems probable since it is abolished by the administration of BAL, containing two sulfhydryl groups[3]. The object of this study was to investigate whether the administration of mercurial diuretics influences the histochemically demonstrable sulfhydryl groups in rat kidney.

Novurit "Medica" (39·5% Hg) was subcutaneously or intramuscularly administered in doses of 10 to 50 mg Hg/kg of body weight to 50 albino rats of the Wistar strain weighing 175–225 g. The rats were killed by decapitation 2–6 h after the administration of Novurit. In the demonstration of protein-bound sulfhydryl groups the method of BARRNETT and SELIGMAN[4] was followed. The reagent, 2,2′-dihydroxy-6,6′-dinaphtyl disulfide, when used in excess at pH 8·5, reacts with

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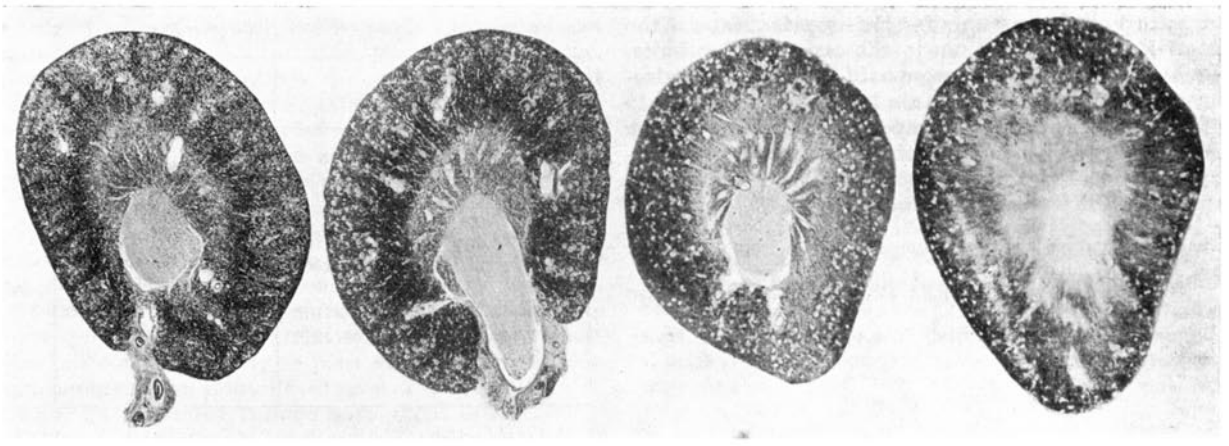

A *B* *C* *D*

A Distribution of –SH groups in normal rat kidney. Section treated according to BARRNETT and SELIGMAN. *B* The same after administration of Novurit (20 mg Hg/kg). *C* Distribution of succinic dehydrogenase activity in normal rat kidney using BT as indicator. Section thickness 80 μ. *D* Succinic dehydrogenase activity after administration of Novurit (20 mg Hg/kg). BT preparation, section thickness 80 μ. Note the almost disappeared activity in the medullary area of HENLE's loops. All 5 ×.

active – SH of fixed tissue proteins to form a colorless substance, which is converted into a colored azo dye by coupling with tetrazotized diorthcanisidine. Furthermore, unfixed frozen sections were treated according to the nitroprusside method of HAMMETT and CHAPMAN[1] and with the ferric-ferricyanide reduction test of LILLIE and BURTNER[2]. Simultaneously the histochemically demonstrable succinic dehydrogenase activity was controlled using blue tetrazolium (BT), 3, 3′-dianisole-bis-4, 4′(3, 4-diphenyl) tetrazolium chloride[3], and neotetrazolium (NT), pp′-diphenylene-bis-2-(3, 5-diphenyl) tetrazolium chloride[4].

Employing the method of BARRNETT and SELIGMAN, the glomeruli of the control animals showed a reddish colour indicating a sparse – SH concentration. They showed no succinic dehydrogenase activity demonstrable with tetrazolium salts. The cells of both proximal and distal convoluted tubules were dark blue, revealing a great concentration of – SH groups. The succinic dehydrogenase activity of the convoluted tubules was also intense. The area of HENLE's loops in the medulla showed by its reddish-blue coloration a somewhat slighter content of –SH groups. In contrast, this area reacted most intensely for succinic dehydrogenase. The intermediate zone between the cortex and the medulla consisting principally of the terminal portions of the proximal convoluted tubules and portions of the HENLE's loops was intensely blue of –SH groups, but this area revealed only slight succinic dehydrogenase activity except in some portions of tubules radiating through it. The collecting ducts in the pyramid showed a weak concentration of –SH groups, whereas succinic dehydrogenase activity could not be observed. The unfixed control sections treated with ferric-ferricyanide test revealed a distribution of the staining intensity similar to that of the sections treated with the method of BARRNETT and SELIGMAN. With nitroprusside test the only observation was that the staining of the medulla was weaker than that of the cortex.

The kidney sections of the rats to which Novurit was administered showed no differences in the distribution and intensity of staining as compared with controls when the BARRNETT and SELIGMAN method, ferric-ferricyanide test and nitroprusside test were employed, although the highest doses were generally lethal. In parallel runs for succinic dehydrogenase activity using BT as indicator, the previously reported inhibition in the enzymatic activity in the medullary area of HENLE's loops could be observed. The enzymatic activity was also depressed in the tubular portions radiating through the intermediate zone. These segments have been regarded as the thick portions of HENLE's loops, but they may equally well be straight terminal portions of the proximal convoluted tubules. The activity of the cortical area was more or less depressed depending on the dose of Novurit. Using NT as an indicator for succinic dehydrogenase, a general decline was noticeable in the enzymatic activity after administration of Novurit. The activity in the cells of HENLE's loops in the medulla was depressed somewhat more than that in the cells of the convoluted tubules. However, such a complete or almost complete lack of staining in the cells of HENLE's loops as observed in the BT preparations could not be established. This difference between the sections stained with BT and NT may be attributed to the much greater sensitiveness of NT as an indicator for succinic dehydrogenase. With NT succinic dehydrogenase activity can be demonstrated in several tissues which remain unstained with BT. Furthermore, NT reacts more rapidly and stains thinner sections more uniformly than BT.

According to our results the potential diminution of –SH groups in the kidney cells after administration of mercurial diuretics could not be demonstrated with the histochemical methods used. This result is not an argument against the assumption that mercurial diuretics act by combining with the essential sulfhydryl groups of enzyme proteins, considering the fact that the vast majority of the demonstrable –SH groups are not concerned with these enzymes. The observation that the most pronounced inhibition of succinic dehydrogenase occurs in HENLE's loops of the medullary area, where the concentration of –SH groups is relatively slight, draws one's attention to the possibility that the proportion of essential –SH groups of succinic dehydro-

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genase to the total amount of -SH groups is greater in the cells of HENLE's loops than in the convoluted tubules. Consequently, the -SH groups of succinic dehydrogenase in the cells of HENLE's loops are more apt to be blocked by mercurial compounds resulting in the pronounced inhibition of this enzyme in the corresponding segments of the nephrons where the concentrative reabsorption of water is believed to begin.

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A. TELKKÄ and K. K. MUSTAKALLIO

Department of Anatomy, University of Helsinki, December 11, 1953.

Zusammenfassung

Es wurde das histochemische Vorkommen und die Verbreitung der Sulfhydrylgruppen sowie die Aktivität der Bernsteinsäuredehydrogenase in den Nieren von Ratten nach Administration von Novurit bestimmt. Die Sulfhydrylgruppen zeigten keine Veränderungen, die Aktivität der Bernsteinsäuredehydrogenase wurde jedoch herabgesetzt, besonders in den Zellen der Henleschen Schleifen.

Prolongation of Clotting Time in the Dormant Bat *(Myotis lucifugus)*

The bat is unique among mammals in that it is essentially poikilothermic when at rest[1]. The rates of the heart beat[2], blood flow[3] and oxygen consumption[4] in the resting bat also vary with the environmental temperature. At low external temperature the red blood cells pass through the vessels either in clumps or rouleaux, but thrombi and stoppage of flow are not seen[3]. At ordinary room temperature (23°C) blood flow is similar to that seen in other mammals. We sought to determine whether changes in the coagulation time of the blood accompany the markedly different physiological states induced by altering the environmental temperature.

Brown bats (*Myotis lucifugus*) were taken from a summer colony in the attic of a farm house in Indiana during the 2nd week of September. The minimum (night) and maximum (day) environmental temperatures during this period were 10°C and 30°C, respectively. Blood clotting times were determined by the capillary tube technic on samples obtained from puncture of a large vein in the web between the tail and hind legs and from the cut carotid artery. Some bats were studied at the time of collection. Other bats were brought to the laboratory and placed in a refrigerator at 5°C. After 16 and 50 days blood samples were taken from some of these immediately upon removal from the refrigerator and from others several days after removal from the cold and maintenance in a room at 23°C.

The results (see Table) clearly show that clotting time is markedly prolonged as a result of exposure of the bat to low temperature and that it becomes short once again when the animal is returned to a warm environment. (There were no significant differences between the clotting times of samples from the tail vein and those from the carotid artery in the same animal.)

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Table.—Blood Clotting Time

Time of test	No. of bats	Minimum	Maximum	Average
On collection	10	1·5′*	24′*	7·4′*
On 16th day at 5°C	4	72′	275′	149′
On 50thday at 5°C	2	170′	210′	190′
On 3rd day at 23°C after removal from 5°C on 16th day	3	8′	40′	26′
On 2nd day at 23°C after removal from 5°C on 50th day	4	10′	30′	19′

* Combination of clotting times from carotid artery and tail vein samples.

We interpret these findings as indicating an adaptive mechanism which prevents thrombus formation during dormancy. Similar results in the hibernating hedgehog[1] and hamster[2] and in the estivating ground squirrel[3] have been interpreted in the same fashion. The present results and those of the experiments just cited indicate that this mechanism is common to all types of mammals that can enter a state of dormancy.

D. E. SMITH, YVETTE S. LEWIS, and G. SVIHLA

Argonne National Laboratory, Lemont, Ill., U.S.A., January 18, 1954.

Résumé

En été, la durée de coagulation du sang augmente notablement si l'on soumet la chauve-souris à une basse température (5°C); elle diminue dès qu'on replace l'animal dans un milieu chaud (23°C). Ceci indique l'existence d'un mécanisme adaptif qui prévient la formation du thrombus.

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Etude de la consommation d'oxygène et de la teneur en acide désoxyribonucléique du foie à divers âges chez le rat

La diminution de la consommation d'oxygène des tissus et des organes avec l'âge a été constatée par divers auteurs parmi lesquels nous citerons HAWKINS[1], PEARCE[2], KAGANOVSKAYA[3], CARROLL[4], ROSENTHAL, BOWIE et GONER[5], SCHULER[6], LAZOVSKAYA[7], CHEYMOL et PELOU[8]. Il convient cependant de rappeler que dans tous ces cas la quantité d'oxygène consommé a été rapportée soit au poids frais, soit au poids sec. Or la constitution des tissus elle-même varie avec l'âge et on

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