Hartnup disease involves mainly the indole group of compounds, and the present cases show primarily imidazole aminoaciduria. The lesion in both diseases is probably one of transport. Studies of the problem are under way. A major difference between the two diseases is the apparent genetic dominance of the aminoaciduria in the imidazole syndrome (*11*).

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Electrostatic Fields: Their Effect on the Surface Tension of Aqueous Salt Solutions

Abstract. Electrostatic fields of up to 7000 volt/cm have been applied across air/solution interfaces by means of parallel-plate electrodes, and the resulting surface tension changes were obtained by measuring, through a balance linkage, the deflection of mica plates floating on the surface. Surface tension changes (always negative) of up to 0.5 dyne/cm have been observed in both distilled water and dilute sodium chloride solutions.

The potential drop which exists naturally at an air/solution interface has received but little attention, particularly when compared to that given the potential distribution at the metal/solution interface. Attempts to measure this potential drop have been made by Frumkin (*1*) and Kamienski (*2*), with conflicting results. Theoretical treatment, including surface concentrations and surface tension changes for solutions of ionic species, has been given by Onsager and Samaras (*3*) and by Falkenhagen and Schmutzer (*4*).

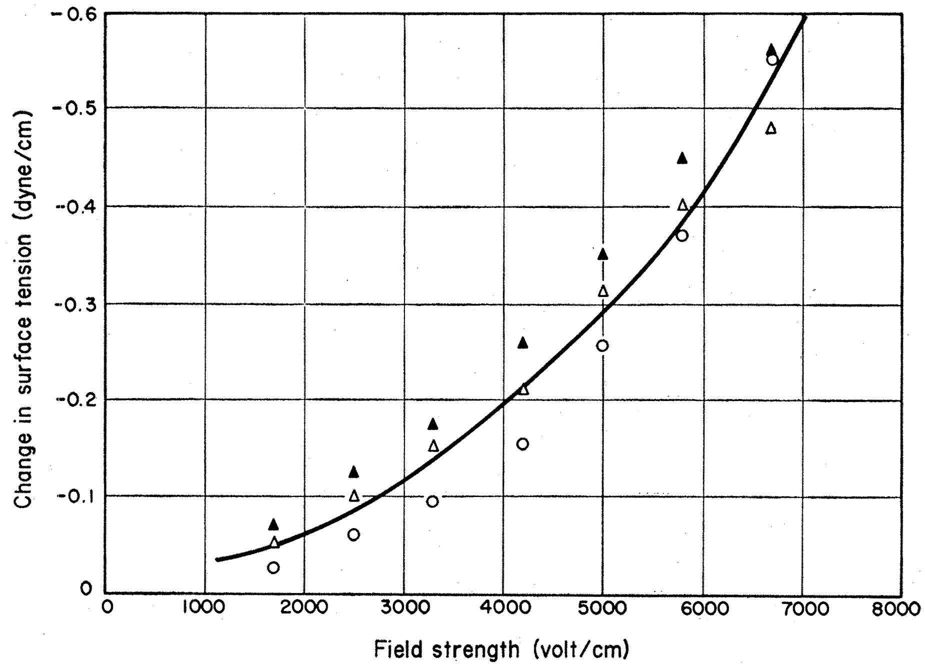

Fig. 1. Changes in surface tension of 3.5-percent NaCl solutions induced by electrostatic fields. Air electrode negative, mica float 7.3 by 12.8 cm, 4.5 cm in between plates; weight of float: solid triangles, 3.903 g; open triangles, 2.296 g; open circles, 1.942 g.

To our knowledge, the influence of impressed electrostatic fields on the potential drop and other properties of the air/solution interface has not been studied at all. As part of a research program supported by the Office of Saline Water, changes in surface tension induced by impressed electrostatic fields of up to 7000 volt/cm have been measured using distilled water and dilute sodium chloride solutions.

The measurements were carried out with a surface energy balance similar in design to one reported by Allan and Alexander (*5*), but modified slightly to permit application of the field across the interface. The movement of a sheet of mica floating on the surface with only one edge inside the field was used to detect changes in surface tension. Calibration by means of force/area curves with films of fatty acids showed a sensitivity of about 5×10^{-3} dyne/cm. Precautions such as complete isolation of the entire apparatus from the laboratory atmosphere and repeated skimming of the surface to remove traces of surface active materials were necessary to obtain reproducible and dependable data.

Application of the electrostatic fields gave rise to forces on the mica float other than the surface tension change. These forces, one a gravitational force due to lifting of the water by the field, and the other an attractive force on the float itself, were corrected for by using floats of various lengths and widths, changing such factors as mass, length of working edge, and area inside the field. It was found that after the proper corrections were made to the measured deflections, a consistent and reproducible force remains, which must be due to a change in surface tension induced by the applied field. The results for a negative air electrode, with 3.5-percent NaCl solutions, are shown in Fig. 1; the three types of points represent runs made with different floats. Similar data have been obtained for other solutions and for the air electrode positive. While there is considerable variation in magnitudes of the surface potential changes, all curves show the same general trend, that is, negative surface tension changes and a slight upward curvature with increasing field strength.

The results of these experiments are interpreted in terms of orientation of water dipoles under the influence of the applied field. If one accepts the value of field strength of 10^7 volt/cm which has been proposed by Kamienski (*2*) as already present in the water/air interface, then it is difficult to understand how application of an external field of less than 10^4 volt/cm can have a measurable influence on the orientation of the dipoles. In view of the measured changes in surface tension, which for electrolyte solutions are quite large, it is reasonable to assume either that the natural field strength in the interface is not nearly so large as proposed by Kamienski, or that a change in some other property (such as ionic concentration) induced by the field is responsible for the surface tension changes. Inasmuch as we obtain significant changes with both distilled water and dilute salt solutions, and since the change in surface tension, $\Delta\gamma$, is negative for both positive and negative fields, we are at present inclined to the former view. This interpretation is also in agreement with that given for results on the influence of impressed electrostatic fields on the freezing of supercooled water as reported recently by Salt (*6*).

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Homograft Reaction in Mice: Effect of Urethane and Sublethal X-radiation

Abstract. Combined treatment of mice with urethane (a nucleic acid antagonist and mitotic inhibitor) plus sublethal x-radiation (500 rad) suppresses the homograft response to a degree considerably greater than that observed with this dose of x-rays alone. Thus, LAF_1 mice receiving two injections of urethane plus 500 rad of x-radiation prior to grafting retained C_3H mouse skin grafts for periods up to 60 days, with a mean graft survival time of 40 days, as compared with 18 days for mice exposed to 500 rad only.

In all animal species studied, it is known that massive doses of ionizing radiation—in the midlethal and supralethal range—are required to suppress the immune response sufficiently to allow the transplantation of genetically foreign, that is, homologous, tissue or cell grafts in adult recipients (see *1*). At lower radiation doses, homograft survival is prolonged, as compared with nonirradiated controls, but the graft is rejected. Very few chemical compounds are known which can mimic this effect of ionizing radiation. In this connection Schwartz *et al.* (*2*) have reported that 6-mercaptopurine (6-MP), a nucleic acid antimetabolite, suppresses humoral antibody production in the rabbit. As a consequence, attempts have been made to alter the homograft response by means of this drug. Thus, Meeker *et al.* (*3*) observed a significant prolongation of skin homograft survival (24 days versus control value of 14 days) in rabbits that received 12 mg of 6-mercaptopurine per kilogram per day for 14 days. However, in mice, similar treatment with this compound did not influence the survival of skin homografts.

In the course of studies on the radioprotective effect of urethane in mice when administered 1 or 2 days prior to x-irradiation (*4*), it became evident that this compound produces a greater depression of the mononuclear cell count in peripheral blood than of the granulocytes. It therefore seemed of interest to determine whether urethane (a nucleic acid antimetabolite and mitotic inhibitor) could modify the response of mice to homografts. The particular question posed in this context was whether the *combination* of urethane plus a sublethal dose of x-radiation could suppress the homograft response to an extent that would allow prolonged survival of homografts, compared to survival in mice exposed to the same dose of x-rays only.

F_1 mice (C57L $\times$ A/He) (so-called LAF_1), 11 to 14 weeks of age, were given two intraperitoneal injections of urethane (1 mg/g) 1 day apart; this was followed 24 hours later by exposure of the mice to a sublethal x-ray dose of 500 rad—250 kv (peak) x-rays at a dose rate of 30 rad/min. Tail skin grafts (*5*) from normal C_3H donors were then prepared and engrafted 1 day after the irradiation. Similar C_3H skin grafts were placed on control LAF_1 mice which received the same x-irradiation only. The criteria employed for evaluating tail skin homografts have been described elsewhere (*6*).

Table 1. Enhanced suppression of homograft reaction in mice by urethane in combination with sublethal x-radiation.

Treatment of recipients	Mean survival time of grafts (days)	No. of surviving grafts/No. grafted				
		At 15 days	At 30 days	At 40 days	At 50 days	At 60 days
500 rad	18	10/10	0/10			
Urethane + 500 rad	40	10/10	6/10	6/10	4/10	0/10
Nonirradiated	14	0/10				

The experimental results are summarized in Table 1. The data show that urethane treatment under these conditions enhances the effect of sublethal x-irradiation in suppressing the homograft response of the host mice. Thus, although the radiation exposure alone increased the skin homograft survival time (from a mean value of 14 days, in the nonirradiated controls, to 18 days), these grafts were all rejected by 26 days. By comparison, in the mice receiving urethane plus x-radiation, none of the C_3H grafts were rejected by 26 days; at 40 days, 6 out of 10 grafts were still intact; at 50 days, 4 out of the 10 mice thus treated still retained intact C_3H skin grafts; by 60 days after grafting, all were rejected. It is to be noted that this considerable prolongation of skin homograft survival (mean survival time = 40 days) occurred under conditions in which the urethane was administered at 2 days and 1 day prior to the sublethal irradiation, and was not given subsequently.

Further evidence that urethane potentiates the suppression of the homograft response when given in conjunction with x-radiation comes from the following observations:

1) Transplantation disease, that is, graft-versus-host reaction, occurred in LAF_1 mice treated with urethane plus 500 rad after the intraperitoneal injection of homologous (C_3H) spleen and lymph nodes cells. Transplantation disease does not occur when C_3H lymphoid cells are administered to LAF_1 mice which have received 500 rad x-irradiation only (*7*). This implies the survival of the injected C_3H lymphoid cells as functioning, immunologically competent cell grafts under conditions of depression of the host's immunological apparatus by the treatment with urethane plus x-rays.

2) Successful bone marrow homo-