

The number of changes of temperature in the breasts of 40 mothers measured at 1 min intervals

Stimulus	Hunger cry			Pain cry			Over	
Minutes	0	1	2	3	4	5	6	7
No. of changes		16	19	19	22	17	15	16
Total			54			54		16

breasts. Figures 1 and 2 show a typical increase of the isotherm area. We observed no decreases of this area.

In 16 cases, the first change occurred 1 min after initiating the hunger cry stimulus whereas in 5 cases the first change was observed only during the pain cry. Of the observed changes, 43.5% occurred during the hunger cry, 43.5% during the pain cry and 13% 1 min after termination of the cry stimulus. Most reactions (22) were noted at 4 min (see Table).

On the control material, only 1 case out of 10 showed a minimal change during the same period of time. All of these 10 cases showed increased isotherm area during the cry stimulus.

**Discussion.** Hunger and pain cries from new-born babies cause an increase of temperature over the breasts of lactating mothers. In this first preliminary study, we exposed mothers to a continuous recording of separate periods of hunger and pain cries. The increase in skin temperature over the breasts was grossly the same during both stimuli. It might have been expected that the pain cry would be experienced by the mothers as an anxiety stimulus and thus decrease the activity in the breasts<sup>7</sup>. But it has been observed that in a healthy baby a long

lasting hunger cry can often get several characteristics of pain cry. Using a combination of hunger and pain cry we cannot be sure that the increase in isotherm area during pain cry may not be a delayed response to hunger cry. We are carrying out further experiments along this line.

The results indicate that it might be important that normal biological communication between mother and child be maintained during the period when lactation is establishing. This means that the mother and the child ought to be together in the maternity hospital at least during day-time (rooming-in) and that the feedings are scheduled according to the infant's cry periods.

**Résumé.** Les résultats d'une analyse thermographique pratiquée sur 40 primipares durant les premiers jours de lactation suivant la naissance indiquent clairement que le cri du nouveau-né cause une élévation de la température dans la zone mammaire.

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<sup>7</sup> M. NEWTON and N. R. NEWTON, *J. Pediat.* 33, 698 (1948).

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## Increased Vascular Permeability in the Primary Cutaneous Allograft Response in the Rat

The allograft response is well established as a cell-mediated immunological phenomenon<sup>1,2</sup>. The grafting of skin is accompanied by an initial acute inflammation evoked by the surgical preparation of the graft bed which includes a short-lived increase in vascular permeability<sup>3</sup>. The development of the subsequent allograft response is accompanied histologically by an intense cellular infiltration, but the presence of further and accompanying changes in vascular permeability has not been studied.

The problem has been investigated in male rats (150–200 g) using inbred strains of Wistar Albino Glaxo and Piebald Variant Glaxo rats as donors and recipients respectively. Orthotopic skin was grafted into round excised wounds ( $9.0 \pm 0.5$  mm diameter) on the flanks of recipient animals, immediately cephalad to the anterior fold of the hind limb. The graft and its bed were protected from external irritation by attaching 'Perspex' wound-healing chambers<sup>3</sup> to the skin surrounding the grafted area; the grafts were held in position and prevented from drying by firmly packing 'Sofratulle' dressing over the graft before the chamber was closed.

Increased vascular permeability was assessed for grafts of various ages by measuring the exudation of circulating Evan's blue injected i.v. (2.5 mg/100 g body wt.) 1 h before the animals were killed. The graft sites were then excised and the exuded dye measured by extraction in

formamide and spectrophotometric estimation<sup>3</sup>. The permeability response associated with the surgical excision of the skin to prepare the graft bed is maximal in 10 min and largely subsides in 30 min although slight exudation persists for some 4–6 h<sup>3</sup>. The insertion of the graft and protective chambers took about 1 h, by which time the initial permeability response had practically subsided.

**Increased vascular permeability in the allograft response.** In the initial 4 days after grafting increased vascular permeability is insignificant (Figure). On the 5th day there is a striking and sudden increase in permeability which extends over the 6th and 7th days and then quickly subsides. It is noteworthy that despite the use of inbred animals, individual rats may show a relatively slight permeability response. Nevertheless the response is well-defined and usually substantial (Figure).

During the well-defined phase of increased permeability the grafts appear healthy macroscopically. A patchy tan-coloured mottling appears between the 9th and 11th

<sup>1</sup> P. B. MEDAWAR, *Proc. R. Soc. B.* 149, 145 (1958).

<sup>2</sup> J. L. TURK, *J. clin. Path.* Suppl. 20, 423 (1967).

<sup>3</sup> A. W. J. LYKKE and R. CUMMINGS, *Br. J. exp. Path.*, 50, 309 (1969).

days and subsequently increases in intensity and extent. By day 15 the grafts have the appearance and consistency of leather; thereafter the rate of destruction of the grafts depends on whether the tissues are kept moist or permitted to dry out by removal of the tulle dressing. Drying grafts fragment quickly, whereas those kept moist with dressing persist for up to 21 days before becoming friable scabs.

In the first 2 days after grafting, the tensile strength of attachment of graft to host bed is negligible but then increases until the 15th day. Tensile strength increases rapidly for grafts aged 5–8 days and then more gradually up to the 15th day.

That the strength of attachment should increase so rapidly during the period of the permeability response

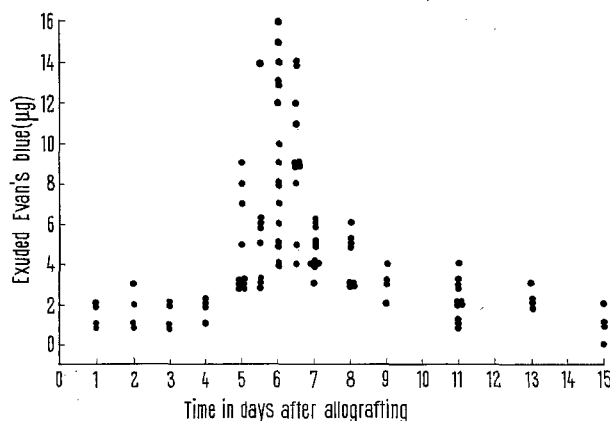
was surprising since the onset of the exudative effects suggested impending rejection. This in fact was the case as revealed by histological examination of the grafts. Histological evidence of rejection began to appear in grafts aged 6–9 days, with progressive increase in the density of mononuclear infiltration in and around blood vessels in the junctional zone between graft and host bed, accompanied by endothelial proliferation and later by intraluminal fibrin plugs. Grafts aged 9–11 days are obviously devitalized.

In conclusion, the allograft response provokes inflammation characterized by a prominent permeability response accompanying the cellular infiltration; the increased vascular permeability precedes macroscopic and histological evidence of rejection<sup>4,5</sup>.

**Résumé.** La réaction cutanée de l'immunité de transplantation contre une greffe allogénique est accompagnée d'une forte mais courte augmentation de la perméabilité vasculaire. La réponse vasculaire apparaît rapidement et cela avant les effets macroscopique ou histologiques de l'immunité de transplantation.

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The time-course of local increased vascular permeability to circulating Evan's blue evoked by cutaneous allografts in the rat. Each symbol represents the result in individual rats.

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## Behaviour of Sodium-Potassium-Activated Adenosine Triphosphatase in Rat Kidney Tissue by Folic Acid<sup>1</sup>

At present it is believed that the sodium pump associated with a membrane-bound ATP-hydrolysing enzyme system, i.e. ( $\text{Na}^+\text{K}^+$ ) ATPase (SKOV<sup>2</sup> and STONE<sup>3</sup>) is mainly localized within the plasma membrane of the mitochondria-rich region in the tubular cell, i.e. within the basal infoldings. Recently BRADE et al.<sup>4</sup> described temporary functional disorders in the rat kidney after administration of folic acid. Electron microscopic studies<sup>4</sup> revealed alterations, especially within the proximal segments of the tubules, with remarkable loss of basal infoldings.

The purpose of the present study was to investigate the behaviour of ( $\text{Na}^+\text{K}^+$ ) ATPase after reduction of basal cell surface in the tubular cells due to folic acid. We used for our experiments a dosage as described by TAYLOR et al.<sup>5,6</sup> to prevent significant cellular damage.

**Methods.** Male Wistar rats<sup>7</sup> weighing 150–200 g were used. The animals were housed in metabolic cages with free access to water. Urine was collected twice daily in 11 h samples, because an action of folic acid was demonstrated with the production of a water-like urine after an oliguric phase post injection. During the experiment food was given every 11 h for 1 h. Experimental animals were sacrificed 63 and 87 h after i.v.

application of folic acid (250 mg/kg body wt.) dissolved in 0.3M sodium carbonate. Control rats remained untreated. Kidneys were removed. The right one was used for light and electron microscopic studies<sup>8</sup> and the left one after determination of wet weight for a homogenate in water (1:11 v/w) prepared in an Ultra Turrax grinder. Aliquots of each homogenate were frozen and lyophilized at  $-26^\circ\text{C}$  for 16 h and stored at  $-31^\circ\text{C}$  until used. No difference for ( $\text{Na}^+\text{K}^+$ ) ATPase activity was noted using

<sup>1</sup> With the support of the 'Schweiz. Nationalfonds zur Förderung der wissenschaftlichen Forschung' No. 4809.

<sup>2</sup> J. C. SKOV, *Prog. Biophys. biophys. Chem.* 14, 131 (1964).

<sup>3</sup> A. J. STONE, *Biochim. biophys. Acta* 150, 578 (1968).

<sup>4</sup> W. BRADE, H. HERKEN and H. J. MERKER, *Naunyn-Schmiedeberg's Arch. Pharmacol. exp. Path.* 262, 228 (1969).

<sup>5</sup> D. M. TAYLOR, G. THRELFALL and A. T. BUCK, *Nature* 212, 472 (1966).

<sup>6</sup> G. THRELFALL, D. M. TAYLOR and A. T. BUCK, *Am. J. Path.* 50, 1 (1967).

<sup>7</sup> Animals kindly supplied by J. R. Geigy AG, Basel (Switzerland).

<sup>8</sup> J. TOHORST, H. P. ROHR and U. SCHMIDT, unpublished results.