control rats without any treatment and in colchicine-treated rats, the few eosinophils found were located in the intravascular space and none of them attached to the endothelial lining (table 2). In estrogen-treated animals, most eosinophils are located in the uterine muscular layers; in colchicine + estrogen-treated animals, most eosinophils are located in the mesometrium (table 3). In estrogen-treated animals, the proportion of extravascular/intravascular eosinophils is much higher in the myometrium than in the mesometrium; in colchicine + estrogen-treated rats this proportion is slightly higher in the mesometrium (table 4). Colchicine drastically decreases the estrogen-induced increase in uterine wet weight (table 1).

Discussion. The disassembly of microtubules by colchicine[10] was suggested as the mechanism to block the migration of leukocytes to the gout[11]. These properties ascribed to colchicine could explain the suppression of estrogen-induced migration of eosinophil leukocytes to uterine stroma and therefore also block estrogen-induced uterine edema.

There are other possible explanations for the suppression of both uterine eosinophilia and uterine edema by colchicine. It has been proposed that colchicine, at a concentration necessary to disaggregate cytoplasmic microtubules, inhibits the release of enzymes mediating the inflammatory response by increasing cGMP levels[12]. The inhibition of prostaglandin E_1 synthesis, release and/or effects[8] might also account for the interaction of colchicine with uterine eosinophilia and edema. It was previously proposed that eosinophils recognize uterine blood vessel endothelial lining after estrogen stimulation[9]. The present results show that colchicine does not block the recognition of uterine endothelial lining by eosinophils, which are attracted to it in estrogen + colchicine-treated animals, but blocks their migration through the vascular wall and also blocks eosinophil migration from the mesometrium to myometrium through uterine stromal extravascular space. Therefore, we suggest that prostaglandin E_1 suppression by colchicine and/or inhibition by colchicine of cGMP increase are not the main mechanisms of interaction by colchicine with eosinophil migration in estrogen action. Instead, we propose that the suppression of cellular mobility by colchicine is the main mechanism of interaction with estrogen-induced uterine eosinophilia which was proposed to mediate edema.

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Allotransplantation of rat parathyroid glands: Effects of organ culture and transplantation into the adrenal gland[1]

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Summary. Allotransplantation of fresh, 1 or 2 week cultured parathyroid glands from Wistar rats (AgB^2) to Fischer rats (AgB^1) resulted in prompt rejection of the transplant in the muscle site; whereas transplantation into the adrenal site offered slightly prolonged survival, suggesting that the latter is a privileged transplantation site.

Culturing of tissues for 3–50 days prior to transplantation has been shown to prolong survival of allografts in some studies[3–7], while other studies have not shown such beneficial effects[8,9]. Transplantation of tissues into several privileged sites such as brain[10], anterior chamber of the eye[11], skin island[12], testis[13], liver[14], spleen and thymus[15] has also been shown to prolong the graft survival.

The present studies1. evaluated the effect of prior culturing for 1 or 2 weeks and 2. evaluated the adrenal gland (AG) as a privileged recipient site for allotransplantation of parathyroid glands (PTG) across a major histocompatibility barrier in inbred rats. Evaluation of the AG as a privileged site was prompted by a fortuitous observation by us in which pieces of a human parathyroid adenoma transplanted into the AG of a rat showed evidence of function for 80 days.

Materials and methods. Wistar furth rats (AgB^2) were used as donors and Fischer 344 rats (AgB^1) as recipients. All recipient rats were surgically parathyroidectomized several days prior to transplantation. Parathyroidectomy was confirmed by serum calcium (Ca) value of less than 7.0 mg/100 ml after an 18-h fast. After removal from the donor, the PTG were cultured at 37 °C in minimum essential Eagle's medium supplemented with 0.03% glutamine and 5% heat inactivated pooled rat serum. The media were changed 3 times a week. The cultures were gassed daily with 95% O_2 and 5% CO_2. For transplantation into the muscle, PTG were placed into a 5×5 mm pocket, created in the right thigh muscles and secured with 4–0 silk. For transplantation into the AG, laparotomy was performed under anesthesia and the left AG exposed. The PTG to be transplanted were placed inside a 22 gauge spinal needle,

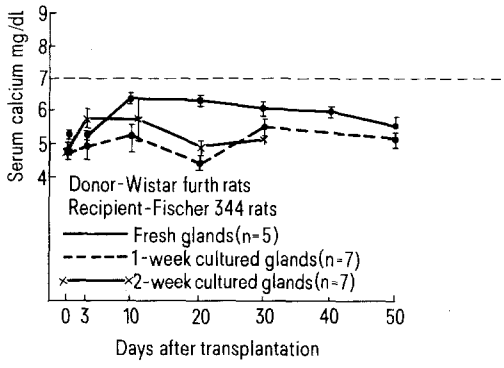

Fig. 1. Effect of allotransplantation of fresh, 1- or 2-week cultured Wistar (AgB^2) parathyroid glands into the thigh muscle on serum calcium of Fischer 344 (AgB^1) rats. Each point represents mean±SE.

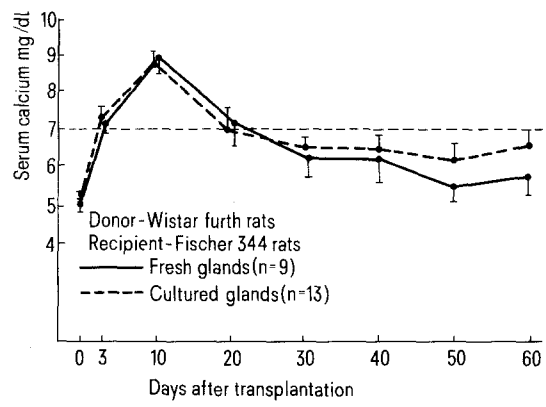

Fig. 2. Effect of allotransplantation of fresh or 1-week cultured Wistar parathyroid glands into the adrenal gland on serum calcium of Fischer 344 rats. Each point represents mean ± SE.

0.25 cm from the tip and the needle was inserted 0.2 cm into the exposed adrenal gland. The pressure was then applied on the stylus of the spinal needle in order to transfer the PTG into the AG. These transplants were subsequently localized histologically to be in the adrenal cortex. The recipient rats were then periodically bled for serum Ca determination. Serum Ca was determined by EGTA titration method[16]. In all the allotransplantation experiments, parallel isotransplantation experiments were also carried out. In the experiments involving cultured PTG, the glands for allo- and isotransplantation were cultured simultaneously.

Results and discussion. Parathyroidectomized Wistar or Fischer rats (without any implantation) maintained their serum Ca to a level below 7.0 mg/100 ml, when followed for a period of 60 days.

Isotransplantation (Wistar to Wistar) of fresh, 1- or 2-week cultured PTG into the thigh muscle resulted in an increase iv serum Ca to a maximum mean value of 9.7±0.7 mg/100 ml, 8.8±0.9 mg/100 ml or 8.5±0.6 mg/100 ml respectively at the end of 30 days following the transplantation. All the animals in the 3 groups showed a decrease in the serum Ca to a value below 7.0 mg/100 ml following removal of the transplant (n=6–8). Similar results were also obtained with isotransplantation of Fischer PTG. These findings indicate that a) isotransplants can survive in the muscle site and b) PTG are viable after 1 or 2 weeks of culturing.

Figure 1 depicts the mean serum Ca values following transplantation of fresh, 1- or 2-week cultured Wistar PTG into the thigh muscle of Fischer rats. None of animals in either the fresh or cultured transplant groups showed an increase in serum calcium to a value above 7.0 mg/100 ml. This observation suggests the rejection of the transplanted PTG before a serum Ca response (to a value above 7.0 mg/100 ml) could be observed in the recipient animals at the time of the first bleeding on the 3rd day after transplantation. Similar early rejection has also been observed in the case of islets of Langerhans when Wistar rats were used as donors and Lewis rats (AgB^1) were used as recipients[17]. Therefore culturing of PTG for 1 or 2 weeks prior to transplantation had no beneficial effect on graft survival in the allotransplantation model tested.

Isotransplantation (Fischer to Fischer) of fresh PTG into the AG resulted in an increase in serum Ca to a maximum mean value of 10.0±0.1 mg/100 ml (n=6) at the end of 30 days following transplantation. Serum Ca decreased to value below 7.0 mg/100 ml in all animals following removal of the left AG containing the transplant.

Figure 2 depicts the serum Ca data following transplantation of fresh or 1-week cultured Wistar PTG into the left AG of Fischer rats. The mean serum Ca values increased to a level above 7.0 mg/100 ml on day 3 in the case of both fresh and cultured PTG. The maximum mean serum Ca values were reached on day 10 in both groups and were 8.9±0.4 mg/100 ml in the case of fresh glands and 8.6±0.5 mg/100 ml in the case of cultured glands. The serum Ca values subsequently decreased to a mean value below 7.0 mg/100 ml by day 30 in both groups. There were no significant differences in the serum Ca values between the fresh and cultured PTG groups at any of the times tested.

The data therefore indicate that, in comparison to the muscle (figure 1), the adrenal site offers slightly prolonged survival of the transplanted PTG. Prior culturing of the PTG however, did not prolong survival in either the adrenal or the muscle site. The mechanism by which the AG functions as a privileged site in the present studies is not known.

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