has lower cytotoxic activity. This finding may be explained considering on one hand the longer the side-chain, the more liposoluble the molecule, the easier the molecule gets into the cells; on the other hand the longer the side-chain is, the less its alkylating capability or, in our opinion, the lower the activation by cell biochemical mechanisms.

Therefore it may be interesting to test the alkylating capability of these diazoacetylglycine derivatives and to synthetize others of intermediate solubility between DGE and DGHA. Moreover, in our opinion, in vivo testing of these substances is indispensable, since while DGA is a good in vivo antineoplastic agent, it has given mild cytotoxic effects in vitro.

Graft-Versus-Host Reaction and Lymphoid Organs in Normally Fed and Protein-Deprived Rats

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Summary. Lymph node graft-versus-host reaction (GVHR) induced by parental splenic lymphocytes inoculated into hind foot pads of F-1 hybrid rats is correlated with the state of the thymus and the spleen of the recipients. This may explain the depression of the reaction after protracted protein deprivation. Furthermore, GVHR provokes mainly in normal rats a reduction of thymus and spleen possibly due to a T-cell transfer to the grafted area.

The graft-versus-host reaction (GVHR) induced in hybrid F-1 rats by parental spleen lymphocytes is deeply impaired if the recipients are deprived of dietary protein. Since the great majority of the cells involved in this reaction are of host origin[2,3] and seem to be formed mainly of T lymphocytes[4], one could suppose that the inhibitory effect of a protein deprived (PD) diet may be conditioned by the involution of the thymus and the decrease in the T cell population induced by this malnutrition. The findings reported here are in favour of this hypothesis.

Adult male (Sherman/Wistar) F-1 rats, derived from pathogen-free strains (C.N.R.S., Orléans), were maintained for 4 or 9 weeks on a PD diet (for its composition, see ref.[5]) while other F-1 rats were fed on a balanced diet. All the rats received, 1 week before killing, an injection into the right hind foot pad of viable spleen lymphocytes obtained from male Sherman donors (1×10^7 for well nourished recipients; 6×10^6 for PD recipients). The viability was determined by a dye (erythrosin) exclusion test[6]. 1 week later, the ratios between the weights and lymphocyte populations of ipsilateral and contralateral popliteal lymph nodes (iPLN and cPLN) were calculated[3,7]. In addition, the weights of thymus, spleen and cervical lymph nodes (not involved in the GVHR) were noted in the grafted rats, and compared with those of non-grafted weight-paired male rats which were either fed on a balanced diet or deprived of protein for 9 weeks.

Results. High iPLN/cPLN ratios were much more frequent in rats with large lymphoid organs than in those with small organs. The correlation was significant as calculated for 38 rats: $r = +0.345$ ($p < 0.05$), $+0.462$ ($p < 0.01$) and $+0.407$ ($p < 0.02$) in regard to the weights of the thymus, spleen and cervical lymph nodes respectively. However, in relation with the latter organs, the percentages of high iPLN/cPLN ratios did not decrease further between the 4 week- and the 9 week-PD groups (Table I).

The weights of the thymi were much lower in grafted rats than in non-grafted ones, fed either on a balanced diet ($p < 0.001$) or on a PD diet ($p < 0.01$). The spleen was also reduced following GVHR ($p < 0.02$) with the former diet but not with the latter one. There were no significant changes in the weight of the cervical lymph nodes.

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Table I. Graft-versus-host reaction (GVHR) expressed as weight- and cell-ratio between ipsilateral (inoculated) and contralateral popliteal lymph nodes. Comparison with weights of lymphoid organs in normally fed or protein deprived rats

Diet	Thymus (mg)	Ratios iPLN/cPLN		Spleen (mg)	Ratios iPLN/cPLN		Cervical lymph node (mg)	Ratios iPLN/cPLN	
		Weight: > 3.0	Number of cells: > 15		Weight: > 3.0	Number of cells: > 15		Weight: > 3.0	Number of cells: > 15
Balanced	280–470	68.7% (11/16)[a]	68.7% (11/16)[a]	520–660	68.7% (11/16)[a]	68.7% (11/16)[a]	6 –19	55.0% (11/20)[a]	60.0% (12/20)[a]
Protein-free (4 weeks)	45–120	41.7% (5/12)	50.0% (6/12)	170–220	50.0% (7/14)	57.2% (8/14)	4.1– 5.5	40.0% (4/10)	40.0% (4/10)
Protein-free (9 weeks)	< 45	20.0% (2/10)	20.0% (2/10)	< 155	0 (0/8)	0 (0/8)	< 4.0	37.5% (3/8)	37.5% (3/8)

[a] Number of rats with GVHR > 3 or > 15 respectively/total number of rats belonging to the different weight groups of each lymphoid organ.

Table II. Weights (mg) of lymphoid organs (means ± SE) in non-grafted rats and in rats bearing a GVHR

Group	Balanced diet				Protein-free diet (9 weeks)			
	Body wt. (g)	Thymus	Spleen	Cervical lymph node[a]	Body wt. (g)	Thymus	Spleen	Cervical lymph node[a]
Non-grafted rats	343.7 ± 7.7 (11)[b]	547.6 ± 25.9	796.5 ± 74.3	17.3 ± 2.8	114.1 ± 1.2 (15)[b]	33.5 ± 3.6	166.3 ± 13.0	4.9 ± 0.9
Grafted rats	357.1 ± 4.0 (16)	379.0 ± 13.2	603.8 ± 12.3	11.8 ± 0.7	112.1 ± 1.3 (8)	20.8 ± 2.5	142.8 ± 7.0	3.6 ± 0.3
Difference (%)		− 37.7[c]	− 28.3[e]	− 31.8 ns		− 37.9[d]	− 14.2 ns	− 26.5 ns

[a] Means obtained from the largest 4 lymph nodes; [b] No. of animals; [c] $p < 0.001$; [d] $p < 0.01$; [e] $p < 0.02$; ns, not significant.

Discussion. The finding of a significant correlation between the weight of the lymphoid organs and the strength of GVHR agrees with the hypothesis that the involution of these organs plays a major role in the dietary inhibition of the host response to the graft, by reducing the supply of T cells involved in the struggle against the grafted cells.

The fact that the GVHR-initiated reduction of the lymphoid organs is less pronounced in PD rats than in normally nourished ones, could be ascribed first to the 'stress' effect of GVHR. Indeed, protein deficiency is by itself a stressing factor as suggested by the increased adrenal and plasma levels of corticosterone in PD rats[8], and the high plasma levels of cortisol in human protein malnutrition[9–11]. This should reduce the sensitivity of the surviving PD lymphocytes to the GVHR stress, since these cells are predominantly cortisone-resistant[12]. However, the decrease in the weight of the thymus and the spleen, observed in grafted rats, is very probably also the consequence of a prolonged transfer of T lymphocytes from the lymphoid organs to the GVHR area in order to compensate the destruction of these cells by the graft. Such a transfer should be, of course, more important with a balanced diet than with a diet deficient in protein.

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Alpha-Tocopherol: Its Inhibition on Human Platelet Aggregation

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Summary. Alpha-tocopherol inhibits human platelet aggregation induced by arachidonate sodium, collagen, epinephrine, adenosine diphosphate or thrombin – arachidonate sodium being the most susceptible. The second phase of the biphasic platelet aggregation induced by epinephrine or adenosine diphosphate is preferentially inhibited.

The generalized Shwartzman reaction (GSR), an experimental model of disseminated intravascular coagulation, can be induced in pregnant rats by means of an α-tocopherol (aT) deficient diet[2]. Conversely, this pathologic condition can be induced in non-pregnant rats by a high lipid diet[3]. These results suggest the possibility of a synergistic mechanism between diets with either a high lipid content or a deficiency of aT in the pathogenesis of GSR in rats. Supplementation with aT to rats on a high lipid diet regularly protects the animals[4].

This report deals with in vitro studies on the inhibitory effect of aT on human platelet function. 9 ml samples of venous blood from healthy volunteers were collected in polystyrene tubes containing 1 ml of 0.1 *M* citrate buffer (pH 6.5) in 2.5% (w/v) of dextrose. Platelet-poor plasma (PPP) was prepared by centrifugation of blood at 1000 *g* for 20 min at 4 °C. Platelet-rich plasma (PRP) was obtained by centrifugation of blood at 300 *g* for 20 min at room temperature. Platelet aggregometry was performed as previously described using a Chrono-log platelet aggregometer coupled to a Fisher Recordall recorder[5]. Briefly, 0.45 ml of PRP was added to a cuvette with a magnetic stirring bar. This was placed in the aggregometer and the light transmission was adjusted to about 10%; similarly that for PPP was adjusted to about 90%. At zero time, 50 µl of normal saline or aT (Arlington Laboratories, Montreal, Que.) were added. 1 min later 50 µl of an aggregating agent were added. Platelet aggregation resulted in an increased light transmission and thus an upward deflection of the recording pen. The aggregating

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