and HL-A haplotype. In allergic families, we more commonly see a high degree of concordance between specific IgE mediated skin sensitivities in allergic siblings who have high levels of total IgE in their serums (*17*). In such family members, and in unrelated populations, genetic regulation of the IgE level is observed as obscuring the effect of specific Ir genes. The IgE regulating gene appears to be just one of the multiple genetic factors affecting expression of the postulated HL-A linked Ir genes, and the problem is further compounded by differences in environmental exposure to allergens (*9, 10*).

At the present time, we believe that neither our extensive family data nor the data of Levine *et al.* and Blumenthal *et al.* are sufficiently clear indications of linkage between Ir genes and HL-A.

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Bias and Marsh state that they would have liked to see the detailed data on all 14 families that entered our study (*1*). As we reported, only the seven families (out of 14) that had ragweed hay fever in successive generations were studied. In the other seven families, only one person had the disease. These families were not studied, as we were interested in the inheritance of the disease as well as of certain immunological parameters—that only about half of our patients with hay fever have family members with the disease is a common finding in our experience. Our original manuscript contained detailed information on three of the seven families studied. The editors asked that the detailed data of the two smaller families be removed in order to save page space. However, the pertinent data for seven families were placed into our table 2 (*1*).

Our conclusion of linkage is based on the data in table 2. Our method was simply comparing the two haplotypes of the propositus in blood relatives of the propositus with regard to occurrence of high avidity IgE antibody to antigen E and clinical ragweed hay fever. Eliminating the propositus from the calculations, and then testing the hypothesis that one haplotype was associated with ragweed pollinosis and the other was not, we found that 13 of 19 blood relatives of the propositus' blood carrying the ragweed-associated haplotype had ragweed hay fever (and strong wheal-and-flare skin reactivity to dilute soutions of antigen E) compared to none of 11 blood relatives of the propositus who carried the other haplotype of the propositus. This difference is statistically significant. These association data indicate genetic linkage. The advantage of comparing the two haplotypes of the propositus in this way is to randomize genetic information contained in other chromosome pairs. Other data in our report concerned immunological specificity of the indicated Ir–antigen E genes, and expression of these genes to include IgG antibody formation, properties that permit comparison to Ir genes in inbred mice.

We suggested that other genetic factors may operate to permit expression of the Ir–antigen E genes, in order to explain why hay fever is common in successive generations of some families, while only occurring sporadically in other families. We suspect that these other hypothetical genetic factors may operate (either directly or indirectly) to control the permeability of allergens (of certain physical sizes and properties) through respiratory mucous membranes. However, no direct studies on these factors are available as yet.

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Locus Coeruleus Lesions and Learning

Crow (*1*) has proposed that the ascending noradrenergic system originating in the locus coeruleus mediates an essential reinforcement component of learning. Anlezark *et al.* (*2*) reported that bilateral lesions of the locus coeruleus in rats deplete cortical noradrenaline and "markedly impair or even abolish" increases in running speed for food reward in an L-maze. If locus coeruleus lesions disrupt an animal's learning capacity as the authors concluded, this deficit should appear in tasks with different performance criteria, for example, an increase in correctly discriminated responses. We investigated the effect of locus coeruleus lesions on the performance of animals in a T-maze discrimination.

Male Holtzman rats with bilateral one-stage or bilateral two-stage lesions of the locus coeruleus were reduced to 85 percent of peak body weight by food deprivation at least 3 weeks after the last operation (*3*). The animals were introduced to a straight runway

Table 1. Summary of noradrenaline concentration and T-maze performance data; S.E.M., standard error of mean.

Group	N	Noradrenaline, cortex and hippocampus (ng/g) (mean ± S.E.M.)	T-maze, days to criterion	
			Median	Range
Control	7	291 ± 15		
One-stage	3	269 ± 19	11	8–16
Two-stage	4	308 ± 20	10.5	6–13
One-stage total lesion	8	52 ± 5	12.5	6–16
Two-stage lesion				
Partial	4	157 ± 17	7	6– 9
Total	3	65 ± 16	7	5– 9

with food reinforcement to habituate them to the general experimental situation. The animals were then given 12 trials each day in a T-maze in which entrance into an arm with an olfactory stimulus (1 percent amyl acetate solution) led to food reward (*4*). The criterion was 22 correct responses in 24 trials. Animals were again given free access to food upon reaching criterion, and behavioral testing ended with measurement of activity by means of an Animex meter (*5*) over a 90-minute period. Throughout the study each lesion group was tested concurrently with a nonlesion control group (*3*). The animals were killed by spinal stem were isolated for subsequent paraf- concussion; the cerebellum and brain- fin embedding and staining with thionin, and the cortex and hippocampus were removed for noradrenaline assay (*6*).

The histological and chemical analyses (Table 1) demonstrated extensive destruction of the locus coeruleus in most animals. In the groups classified as having total lesions, only two animals had any identifiable locus coeruleus cells remaining. The reduction in cortical noradrenaline ranged from 67 to 90 percent in these animals. The one-stage bilateral lesions markedly debilitated the animals; ataxia, temporary aphagia, and urogenital disorders were observed (*7*). Postoperative recovery in the animals with bilateral two-stage lesions was both more rapid and more complete.

During the habituation trials, all animals increased their running speeds so as to complete the 120-cm runway within 5 seconds. The running speeds for the animals with lesions were consistently lower than those for the control animals; however, we attribute this to motor variables. Motor difficulties observed (*7*) in some animals in all the lesion groups may have restricted their maximum running speeds. Activity, as measured during the 90-minute test period, was positively correlated with noradrenaline content (group with single-stage lesions and corresponding controls, $r = .82$; group with two-stage lesions and controls, $r = .67$). The motor disturbances and decreased activity in the animals with lesions may account for their slower speeds in the runway.

Running speed in the T-maze was not a limiting variable because the criterion was based on entrance into the goal arm rather than speed of traversal. There was no initial preference for the olfactory cue. The animals with bilateral single-stage lesions did not differ from their controls with respect to days to criterion (Table 1) [Mann-Whitney: $U = 11$, $P = .92$ (*8*)]. There were no significant differences for this measure for the group with total two-stage lesions, the group with partial two-stage lesions, and their controls [Kruskal-Wallis: $H_c = 2.13$, $P > .1$ (*8*)]. These results fail to demonstrate a learning deficit in a T-maze discrimination despite a substantial decrease in cortical noradrenaline caused by bilateral locus coeruleus lesions.

If the nucleus locus coeruleus is the substrate for a reinforcement system operative in appetitive learning, destruction of the nucleus should lead to deficits in any learning task with food reward. Since animals with complete bilateral lesions of the locus coeruleus can learn a T-maze discrimination, we conclude that the structure is not an essential component of a common reinforcement system.

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Chlorine Compounds and Stratospheric Ozone

The potentially serious impact of man-made chlorofluoromethanes (CF_xCl_y) on stratospheric O_3 is now documented in the scientific literature (*1–3*). In our recent report (*2*) we showed that the potential size of this atmospheric perturbation is large, so large that chemical control of the stratosphere will eventually pass to the chlorine oxides (ClO_x) that arise from CF_xCl_y usage. According to our calculations, the ClO_x sink for stratospheric O_3 can be expected to dominate natural sinks for O_3 by 1985 or 1990. This time dependence is striking. Time scales of decades arise from our current knowledge of atmospheric mixing rates, and from the present belief (*1–3*) that the only significant mechanism by which nature can break apart CF_2Cl_2 and $CFCl_3$ is by stratospheric photodissociation brought about by ultraviolet radiation.

One purpose of this technical comment is to facilitate the readers' efforts