pounds, from either living or dead organisms, is inevitable, and the evolution of protective mechanisms against the more potent of these compounds may have been necessary. Destruction of a compound in the medium would be the most direct way to prevent it from disrupting the organism's normal regulatory mechanisms. It appears that the excreted phosphodiesterases of *Dictyostelium* and *Physarum* may be examples of a functional class of enzymes that protect an organism from the damage that would result from an exogenous source of a compound that participates in the regulation of the organism's metabolism or development.

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Allergic Encephalomyelitis: New Form Featuring Polymorphonuclear Leukocytes

Abstract. *The passive transfer of allergic encephalomyelitis can be produced in a single day. In work described, the procedure was made to coincide with a transient drug-induced deficiency of lymphocytes. As a result, the lesions of this autoimmune disease contained a predominance of polymorphonuclear leukocytes instead of the usual mononuclear cells. Not only is this a new histologic form of the disease, but the ready recognition of polymorphonuclears as reactive cells provides a powerful new tool for investigating the roles of immunologically specific effector cells and nonspecific reactive cells in production of tissue damage.*

The perivascular inflammatory exudate of the autoimmune disease experimental allergic encephalomyelitis (EAE), like other forms of delayed hypersensitivity, contains far more mononuclear than polymorphonuclear leukocytes (*1*). Further dissection of the composition of the infiltrate can be accomplished with passive transfer of EAE by injection of lymph node cells from immunized donors into normal, unimmunized recipients. With the aid of this technique, it has been found that specifically sensitized mononuclear cells from the donor are far less common in the EAE lesions than nonspecific mononuclears from the donor or from the recipient (*2*). The importance of nonspecific host cells is indicated also by suppression of passive transfer of EAE by cytotoxic drugs or radiation applied to the *recipients* in advance of the cell transfer (*3*). We report a particular treatment of the recipient that has produced a morphologically new form of passive EAE in which the inflammatory leukocytes are predominantly polymorphonuclear. These polymorphonuclears can be of host origin only.

The method was based on three considerations. First, the passive transfer system permits manipulation of the recipient without affecting the encephalitogenic potency of the donor cells. Second, the cytotoxic drug cyclophosphamide reduces the level of circulating mononuclears faster than it reduces the level of polymorphonuclears (*4*). Therefore, it is easy to obtain a transiently selective lymphopenia in the recipients. Third, the lesions of EAE can be detected in a scant 24 hours after passive transfer if recipients are prepared by a physical injury of their brains which lowers the threshold of disease (*5*). This rapid transfer of EAE can be accomplished during the period of selective lymphopenia.

Donor female Lewis rats (Microbiological Associates) were immunized in the right hind feet with guinea pig spinal cord, Freund's complete adjuvant, and pertussis vaccine (an ancillary adjuvant) (*5*). Seven days later, when many animals had early clinical signs of EAE, the draining lymph nodes were harvested and processed into a cell suspension. The living cells were injected intravenously into unimmunized, histocompatible male Lewis recipients. The recipients had been prepared beforehand with thermal injuries of the brain, and some of them had been given cyclophosphamide intraperitoneally. The recipients were killed 24 hours after passive transfer, and their brains were examined histologically.

In the control recipients that did not receive cyclophosphamide, veins and brain parenchyma adjacent to the zone of thermal coagulation necrosis were heavily infiltrated with mononuclear cells (*5*). These EAE lesions were identical with those observed in the usual protracted forms of EAE. In recipient rats that were given cyclophosphamide (125 mg/kg) 1 day before cell transfer, the location of the lesions was unchanged, but mononuclear cells were reduced in number and were largely restricted to the walls of a very few veins. In their place, polymorphonuclear leukocytes were present in large numbers (*6*). These cells were observed in vessel lumens, walls, and perivascular

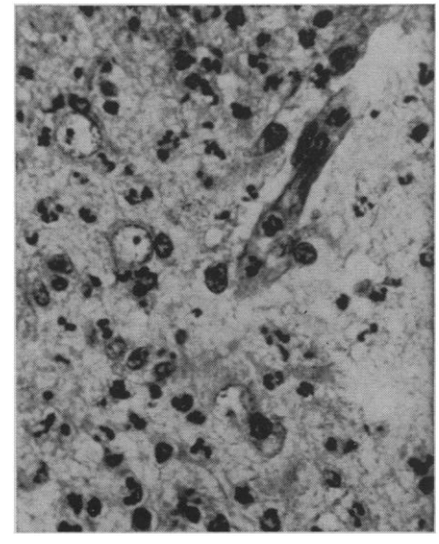

Fig. 1. The new form of allergic encephalomyelitis. There are four polymorphonuclear leukocytes in the lumen of a capillary (upper right), and at least 50 others are recognizable in the brain parenchyma of this one field. The large, pale nuclei with prominent nucleoli are neuronal. Medium-sized nuclei are probably mostly glial. Inflammatory mononuclear cells, which characterize conventional forms of EAE, are rare. Periodic acid–Schiff–hematoxylin stain (× 680).

spaces, but especially in brain parenchyma (Fig. 1). They had to be of host origin because donor lymph node suspensions had few or no polymorphonuclears. Smaller and larger doses of cyclophosphamide (75 or 200 mg/kg) were effective but the lower dose allowed the emergence of somewhat more mononuclear cells. Administration of the drug 2 days before cell transfer decreased the polymorphonuclear infiltration somewhat, and treatment 3 or 6 days before transfer inhibited it completely so that there were no EAE lesions of any type. The occurrence of lesions with polymorphonuclears corresponds to the period of selective lymphopenia before pancytopenia prevails after cyclophosphamide treatment (*4*). Thermal injuries 2, 3, or 6 days before cell transfer were satisfactory, but the 3-day interval was optimum. Neither polymorphonuclears nor mononuclears were observed adjacent to thermal injuries, regardless of whether or not cyclophosphamide had been injected, provided that lymph node cell transfer was omitted or replaced by serum from donors with EAE, or replaced by cells from donors immunized with nonneural tissue (adrenal) and adjuvants (*7*).

Two additional experiments proved that the polymorphonuclear infiltrates were the direct consequence of the immunological activity of donor EAE cells. First, neither polymorphonuclear nor mononuclear leukocytes appeared when cyclophosphamide-treated recipients were given 0.2 mg of guinea pig myelin basic protein intravenously 1 hour after the lymph node cell transfer. This is in accord with the previous demonstration of immunologically specific inhibition of EAE by basic protein, probably due to a type of desensitization (*8*). Second, neither polymorphonuclear nor mononuclear infiltrates were produced when Lewis EAE cells were administered to appropriately prepared but *histoincompatible* BN rats. This agrees with the failure of passive transfer to cross major histocompatibility barriers unless the recipient is rendered tolerant of donor transplantation antigens (*9*).

Although it is likely that host polymorphonuclear cells have responded in our system simply because the host had few functioning mononuclear cells, the mechanism involved is unknown. Also, it is uncertain whether the few mononuclear cells found in the lesions are the immunologically specific donor cells, unsensitized nonspecific donor cells inadvertently included in the EAE lymph node suspension, or host mononuclear cells that have escaped the cyclophosphamide effect. As these problems are resolved, the new form of EAE should be useful for deciphering the manner in which specific and nonspecific lymphoid cells cause injury in autoimmune diseases and other forms of delayed hypersensitivity.

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1. The hyperacute form of EAE is an exception [S. Levine and E. J. Wenk, *Science* **146**, 1681 (1964)]; the large numbers of polymorphonuclear leukocytes in this condition appear to be related to its extreme severity and are accompanied by edema and fibrin exudation. Neither the histology nor the manner of production suggest an intimate relation to the new form of EAE presented in this report.
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6. Polymorphonuclear leukocytes were increased in absolute numbers and were not merely increased in relation to the sparse mononuclear cells. This was obvious on inspection and was confirmed by cell counts. With the aid of an ocular grid, an area of 0.0335 mm² was studied in seven high-power fields from five rats with the new form of EAE and in 14 fields from five control rats with conventional EAE. The fields selected for study were areas of heavy inflammatory infiltration adjacent to the thermal injury. The controls had only two to ten polymorphonuclear cells in the grid area (average 5.5) amid the large numbers of mononuclear cells. The new form of EAE had 29 to 78 polymorphonuclear cells in the same area (average 55).
7. A few polymorphonuclear cells occurred within the necrotic brain tissue, independent of the administration of drug and cells. This was of no importance because EAE lesions of whatever type occupied the adjacent viable tissue and not the dead cerebral debris.
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Promising Catalyst for Auto Exhaust

For some time we have been studying the transition element oxides, in particular the perovskites and the tungsten bronzes, for activity as heterogeneous catalysts. Therefore Meadowcraft's (*1*) report that $Sr_{0.2}La_{0.8}CoO_3$ rivaled platinum at the aqueous oxygen electrode has led us to test $LaCoO_3$ itself for activity in the gas phase. We now report that it does appear to rival platinum in the gas phase as well and suggest that it should be tested as a potential auto exhaust catalyst. Meadowcraft (*1*) estimates that the cost of this catalyst would be about $1 per pound.

Table 1. Catalytic activity of $LaCoO_3$ (1.7 with a specific area of 1.4 m²/g) from 25° to 450°C. The minus sign indicates that no peak was detected; F.G., feed gas. Flow rate was measured in cubic centimeters per minute.

T (°C)	Flow rate (cm³/min)	Mole percent						
		CH_4	C_2H_6	C_2H_4 or C_3H_8*	C_4H_{10}	1-Butene	*trans*-Butene	*cis*-Butene
25	F.G.	—	—	0.006	0.377	0.831	2.301	96.482
25	13.2+	—	—	0.032	1.756	0.813	2.568	88.987
25	F.G.	—	—	0 002	1.133	0.888	3.727	94.246
25	4.5+	—	—	0.004	4.033	2.455	6.803	86.703
50	4.5	—	—	0.003	8.687	5.983	12.992	72.333
75	4.5	—	—	0.001	13.144	6.242	14.590	66.021
100	6.0	—	—	0.005	21.770	10.462	25.271	42.467
125	5.7	—	—					
	F.G.	—	—	—	8.587	0.474	5.259	85.676
150	7.2	—	0.001	0.057	75.294	1.001	5.480	18.162
180	6.6	—	0.022	1.994	71.808	0.442	8.911	16.817
200	6.6	0.782	0.403	1.960†	69.024	0.777	9.152	17.897
230	4.2	10.371	2.981	6.087	55.075	0.683†	7.272	17.525
260	3.9	14.190‡	4.584‡	6.443	29.461	4.215	7.169	33.933
270	3.3	31.145‡	8.332‡	9.390	10.362	0.144	4.558	9.381
	F.G.	—	—	0.025	4.275	0.177	0.756	94.763
300	5.7	23.013‡	7.378†‡	8.987	36.657	0.932	4.677	18.349
325	5.7	30.494‡	16.809‡	10.407	26.470	1.337	4.360	10.110
350	4.2	37.070‡	14.299‡	11.384	27.603	0.761	3.013	5.866
375	8.4	36.400‡	16.158‡	10.535	21.550	2.370	4.895	8.086
425	7.2	32.103‡	8.150‡	7.589	29.938	2.972	8.705	10.538
450	7.8	12.626‡	3.127‡	4.657	42.402	5.254	14.541	17.388

* Identification uncertain. † Peak areas estimated. ‡ Overlapping peaks.