identical in their capacity to stimulate or respond in MLC.

Thus serum 1 in these two families marks a common MLC gene product, or LD factor, though this is associated with HL-A1 and W17 in family F, and HL-A3 and W5 in Ruth's family. It is reasonable also to assume that serum 2 is marking the MLC region of the haplotype HL-A2, W15, although our data only show that it is not marking the HL-A antigens that this serum was known to detect by the cytotoxicity test, but a factor that segregates with HL-A. The ABCIL procedure as reported in our study may provide a rapid serological approach to the detection of LD factors and is now being used to investigate the correlation between ABCIL reactivity of certain selected serums and stimulation in unidirectional MLC in unrelated individuals.

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6. For this procedure, 0.2 ml of diluted serum (1 : 4) was absorbed with 20×10^9 lymphocytes or 0.2×10^9 platelets at room temperature for 1 hour, twice.
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9. Eleanor's cells responding to Laurie's mitomycin C-treated cells (EL_m) gave an S.I. of 1.95 to 2.4. The S.I. values for LE_m, EB_m, BE_m, BL_m, and LB_m were 1.9 to 2.3, 1.9 to 6.5, 1.4 to 2.6, 0.5 to 0.9, and 0.8 to 1.0, respectively.
10. We thank the family under study for their interest and participation, National Institutes of Health for supplying many of the serums, and J. Kijewski for technical assistance.

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Dendritic Spine "Dysgenesis" and Mental Retardation

Abstract. *Golgi studies reveal abnormally long, thin spines and the absence of short, thick spines on dendrites of cortical neurons in retarded children with normal karyotypes. The degree of dendritic spine loss and abnormality appears to be related to age and the severity of developmental retardation. Dendritic spine "dysgenesis" is a common feature of the microstructural pathology that occurs in profound mental retardation of unknown etiology.*

Dendritic spines originally described by Cajal in Golgi preparations are postsynaptic targets for a major proportion of the synaptic inputs to pyramidal and spiny stellate neurons of the cerebral cortex (*1*). The significance of the relation between dendritic spines and synapses has not been fully exploited in studies of human neuropathological processes, particularly in conditions that yield few specific findings in routine microscopic studies despite clinical evidence of severe cognitive and behavioral deficits. Such conditions are frequently encountered in infants and children with profound mental retardation.

Marin-Padilla (*2*) first described dendritic spine abnormalities in two infants with trisomic chromosomal anomalies known to be associated with mental retardation. In a recent study I also observed unusual dendritic spines in an infant with seizures and mental retardation of unknown etiology (*3*). This observation called into question the specificity of dendritic spine abnormalities in chromosomal disorders and prompted the Golgi study reported below of cortical dendritic spines in retarded children or infants with normal karyotypes.

The rapid Golgi method was applied to small blocks of unfixed or fixed (with formalin or glutaraldehyde) cerebral cortex tissues from 30 pediatric autopsy cases. These included six infants and children between 3 months and 12 years of age with profound mental or motor retardation (or both) in whom no etiological factors could be defined as a basis for their severe developmental deficits (*4*). A small block of cortical tissue was also obtained from a 10-month-old retarded child (who is still alive) during brain biopsy performed for the purpose of diagnosis and family counseling. Mild to moderate microcephaly was noted in four other subjects and clinical seizures in three, but there was no correlation between microcephaly and seizures (*4*). Cortical tissue was obtained postmortem from 24 pediatric deceased patients who had normal developmental and neurological histories and these tissues were used for evaluating presumably normal characteristics of cortical dendritic spines and spine distribution at different ages.

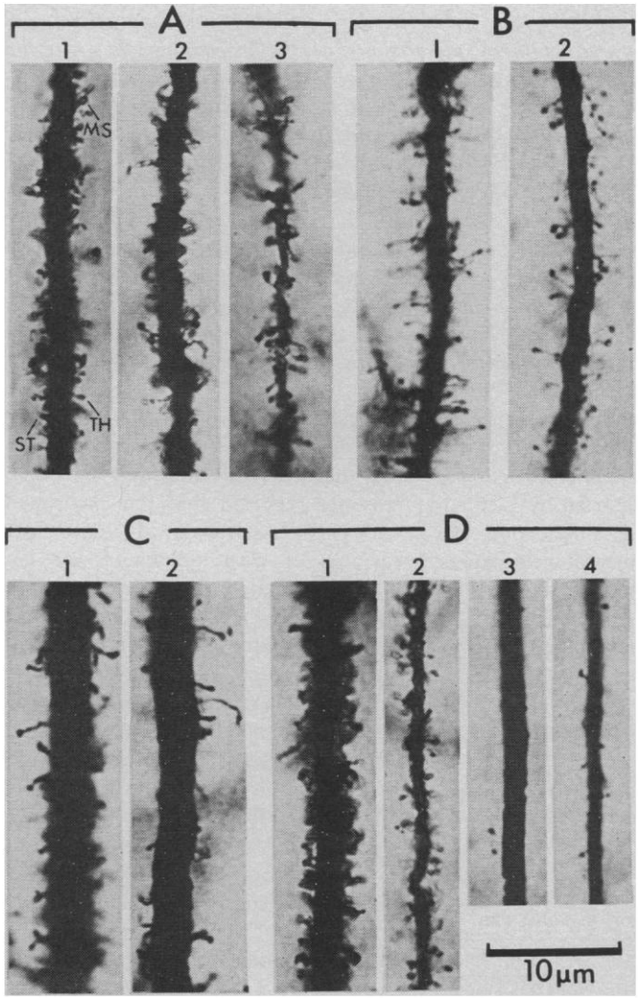
Peters and Kaiserman-Abramof (*5*) identified three basic types of dendritic spines on pyramidal neurons in Golgi and electron microscope studies of the adult rat parietal cortex: stubby (ST), mushroom-shaped (MS), and thin (TH) spines. Similar types are also identifiable in different proportions on different dendritic segments of neurons in human cerebral cortex. As shown in Fig. 1, A1 and A2, and Fig. 2, A1, proximal apical dendritic segments from motor cortex pyramidal neurons in a neurologically normal 6-month-old infant exhibit a preponderance of ST and MS spines. Basilar dendrites and distal apical dendritic segments have a high proportion of TH spines (Fig. 1, A3), in agreement with Peters and Kaiserman-Abramof (*5*).

Dramatically different spines are observed on proximal apical dendritic segments in cortical tissue from the brain biopsy of a 10-month-old retarded child (Fig. 1B). In addition to an absence of ST and MS spines a predominance of unusually long (4 to 8 μm), very thin spines with prominent terminal heads is observed. Electron microscope studies of the tissues of this patient confirm the presence of long, thin spines in synaptic relation with morphologically normal presynaptic axonal terminals. The contrasting features of typical apical dendritic segments from the normal 6-month-old infant and the 10-month-old retarded infant are illustrated in camera lucida drawings (Fig. 2A). The entanglement of long, thin spine pedicles on large dendritic processes is particularly striking in the preparations from the retarded child. The finding of abnormal dendritic spines in Golgi preparations of glutaraldehyde-fixed fresh tissue removed at cortical biopsy rules out a contribution of postmortem artifact.

Two slightly younger retarded patients (7 and 9 months old) with normal karyotypes showed abnormal cortical dendritic spines similar to those of Fig. 1B. Examples of proximal apical dendritic segments of large and medium pyramidal neurons of the motor cortex from a profoundly retarded 3-year-old child (normal karyotype) are shown in Fig. 1C. Variable reduction of all types of spines is evident, but there is relative preservation of very long, thin spines.

The oldest retarded patient in this series was a 12-year-old child who had seizures and who had shown arrested behavioral development approximately equivalent to that of an 8-month-old infant (*4*). Golgi studies revealed many neocortical neurons with dendrites that appeared rigid and that were almost totally devoid of ST and MS spines (Fig. 1, D3 and D4). However, a few very thin spines with barely detectable necks were observed on most dendrites. The extraordinary change in overt characteristics of apical dendritic spines in the preparations from the 12-year-old retarded patient is apparent in comparison with dendritic segments from a normal 7-year-old child who sustained a fatal burn accident (Fig. 1, D1 and D2). Camera lucida drawings of typical dendrites in these two subjects are shown in Fig. 2B. A few normal MS and ST spines remain on the apical dendritic segment of the 12-year-old retarded patient, but many of the thin spines have very thin necks and enlarged, irregular terminal heads (Fig. 2, B2).

The proportion of well-impregnated pyramidal neurons exhibiting a particular type of spine abnormality (such as spine loss or long, thin spines) varied from case to case. Variations were also observed in any one case depending on the cortical area examined (such as motor cortex, visual cortex, or hippocampus) and the location of neuron cell bodies. Not infrequently, two



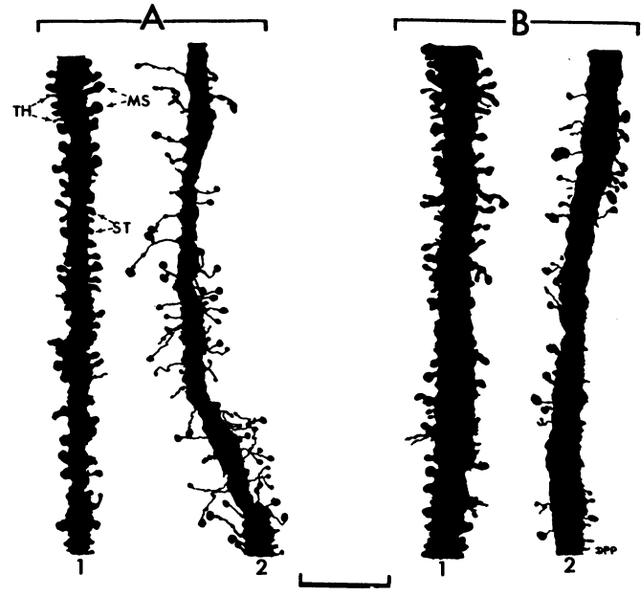


Fig. 1 (left). Rapid Golgi preparations of dendrites of motor cortex neurons in normal and profoundly retarded subjects. (A) Normal 6-month-old infant with negative neurological history, postoperative death. (A1 and A2) Proximal apical dendritic segments of medium-sized layer V pyramidal neurons. Three basic types of dendritic spines are identified: thin (TM), stubby (ST), and mushroom-shaped (MS) spines. (A3) Basilar dendritic segment with a predominance of TH spines. (B1 and B2) Proximal apical dendritic segments of medium-sized pyramids in frontal cortex of a 10-month-old retarded child (brain biopsy case; infant still alive). Abnormally long, thin spines predominate; many appear entangled. There is a marked reduction in MS and ST spines. (C1 and C2) Proximal apical dendritic segments of medium pyramidal neurons in motor cortex of a 3-year-old retarded child. Note variability in extent of spine loss and distribution of abnormally long, thin spines. (D1 and D2) Proximal and distal segments of apical dendrites, from a normal 7-year-old child (accident case). (D3 and D4) Examples of apical dendritic segments from a 12-year-old profoundly retarded child. A few TH spines are seen but otherwise there is almost complete absence of spines. Fig. 2 (right). Camera lucida representations of rapid Golgi preparations showing typical dendritic segments of medium-sized pyramidal neurons of motor cortex in normal subjects and profoundly retarded subjects. (A1) Nonretarded 6-month-old infant. Three basic types of spines are identified: thin (TH), stubby (ST), and mushroom-shaped (MS) spines, as in Fig. 1A. (A2) Dendritic segment from a 10-month-old retarded infant (biopsy). The remarkable length of the fine and sometimes entangled spines with prominent terminal heads is evident. Multiple varicosities on pedicles of these long, thin spines are occasionally seen. The MS and ST spines are rare. (B1) Normal 7-year-old child (accident case). Apical dendritic segment from same area of cortex as in Fig. 1, D1. (B2) Apical dendritic segment from a 12-year-old profoundly retarded child. The paucity of MS and ST spines and the presence of thin spines with abnormally expanded terminal heads are striking features of dendritic spine abnormalities in this advanced case of profound retardation. The bar is 10 μm.

adjacent pyramidal neurons with similar dendritic branching patterns and apical dendrites in the same plane showed different degrees of spine loss and spine abnormality. In general, there was no obvious relation between the degree of dendritic spine abnormality in these elements and dendritic length or branching patterns. Dendritic spine abnormalities seemed to be more closely correlated with the severity of retardation and age of the subject than were changes in basic dendritic geometry. Apropos of this is a recent report that dendritic branching is somewhat reduced in preparations from young, but not older, retarded patients (*6*).

This study demonstrates two types of dendritic spine abnormalities in retarded children with normal karyotypes: dendritic spine loss and the presence of very long, thin spines that resemble the developing spines of primitive neurons (*2*). The functional significance of these abnormalities is not known. However, it is reasonable to expect that spine loss and alterations in dendritic spine geometry (*7*) exert significant effects on integrative operations of dendritic systems as receptor surfaces for synaptic inputs to cortical neurons (*1, 8*). The emphasis here on dendritic spine "dysgenesis," which implies defective development, as a common feature of the microstructural pathology in profound mental retardation affirms the importance of axodendritic synaptic dysfunction in many developmental disorders of infancy and childhood (*2, 9*).

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Synergism of Insecticides by Herbicides: Effect of Environmental Factors

Abstract. *The synergism of parathion and* p,p′*-DDT* [*1,1,1-trichloro-2,2-bis-(p-chlorophenyl)ethane*] *by atrazine was investigated as a function of soil type, age of pesticide soil residues, and the presence of soils in quiet or turbulent water. Compared to previous tests in which the pesticides were applied on glass surfaces, a significant reduction of the toxicity of the insecticides to fruit flies and of the synergistic effects of atrazine was observed with soils, particularly a silt loam. The effects of atrazine as a synergist in soil declined rapidly within 4 days. The toxicity of parathion in water and its synergism by atrazine were significantly reduced by soil sediments, depending on the type and amount of soil present. Soils were highly effective in turbulent water: in water containing the relatively high parathion concentration of 0.3 part per million, 93 percent of the mosquito larvae present died within 24 hours, yet this solution was rendered nontoxic by being mixed with 5 grams of a loam soil. With atrazine present in the latter system, however, 38 percent of the mosquito larvae died. Thus, insecticides can be more or less toxic, depending on their concentrations, the presence of synergists, and the environmental conditions.*

Synergism of insecticides by herbicides, resulting in enhancement of the toxicity of selected insecticides to three insect species, was reported by Lichtenstein *et al.* (*1*). This publication was picked up by a number of newspapers, one of which (*2*), under the heading "Warning given on insecticides," reported that "farmers who use both insecticides and herbicides on their crops may be applying more insecticides than they need." While this may be true, it was not reported that the experiments with pesticides were conducted on glass surfaces or with tap water. We have now investigated the synergism of insecticides by herbicides under more realistic conditions to determine the effects of some environmental factors. We report here the effects of soil type, age of pesticide soil residues, and the presence of soils in quiet and turbulent water on the synergism of parathion and *p,p′*-DDT [1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane] by atrazine.

Table 1. Effect of soils and water turbulence on the synergism of parathion toxicity to mosquito larvae (*Aeddes aegypti* L.) by atrazine in water solutions. Amounts and concentrations used were: water, 20 ml; soil, 5 g; atrazine, 10 ppm; parathion, 0.015 ppm. Results are means of three replicated tests.

Pesticide	24-Hour mortality (%) of larvae in water with		
	No soil	Sand	Loam
Atrazine			
No mixing	0	0	0
Mixing		0	0
Parathion			
No mixing	20 ± 7*	18 ± 4	5 ± 4
Mixing		5 ± 4	0 ± 0
Atrazine + parathion			
No mixing	73 ± 18*	71 ± 14†	64 ± 4‡
Mixing		18 ± 4†	0‡

* Difference significant at $P = .01$ by Student's t-test. † Difference significant at $P = .01$. ‡ Difference significant at $P = .001$.

To determine the toxicity of the insecticides in soils, fruit flies (*Drosophila melanogaster* Meigen) were exposed directly to pesticide-treated soil. For this purpose, 10-g portions of air-dried soil were placed into 4-ounce (~ 120-ml) test jars and treated with chloroform solutions of parathion, *p,p′*-DDT, atrazine, or combinations thereof. After evaporation of the solvent (*3*), 50 fruit flies were introduced into each jar and held for 24 hours, when mortality counts were made. Each treatment was replicated three times. To determine the per-