non of lectin release appears to be independent of seed viability. Soybean seeds characteristically lose their capacity to germinate relatively rapidly within a few years of storage (*10*). Using the qualitative filter-paper assay, we have tested such viable and nonviable seeds of the soybean varieties noted earlier for lectin release with identical results—lectin is released regardless of germination capacity.

Perhaps the most significant aspect of early lectin release by soybean seeds is an observed insensitivity to sodium azide, a potent inhibitor of oxidative phosphorylation and cellular metabolism. At azide levels of 0.02 percent (3.08 m*M*) and 0.2 percent (30.8 m*M*), which completely inhibit the germination response of viable soybean seeds and which far exceed azide levels that produce anomalous germination effects in some legume seeds (*11*), the lectin-release phenomenon is still evident (Fig. 3c). Such azide concentrations had no effect on the endpoint (hemagglutination titer) of agglutination induced by purified soybean agglutinin. Azide insensitivity may suggest that the mechanism by which soybean lectin is released from the seed in the early phases of hydration may differ radically from other known seed protein export systems. In the barley aleurone system, for example, where certain hydrolases are exported from the aleurone layer of the endosperm in response to gibberellic acid, the appearance of enzyme activity is sensitive to inhibitors of oxidative phosphorylation (*12*) and requires de novo protein synthesis (*13*), activation of phospholipid biosynthesis (*14*), and elaboration of endoplasmic reticulum (*15*) and membrane-bound polyribosomes (*16*), ostensibly for the purpose of compartmentation and transport of the enzymes to be secreted. Soybean lectin, in contrast, is detectable in dry seeds, and its appearance during hydration is presumably the result of activation of a preexisting stored protein fraction. While its localization within the seed is probably chiefly confined to cotyledonary tissue (*17*), it is apparently not associated with the protein bodies in cotyledonary cells where the 7*S* and 11*S* "glycinin" storage proteins reside (*18*). Our observations of an insensitivity of lectin release to azide, and a similarity in changes in lectin activity between seed-associated lectin and lectin outside the seed, may indicate that soybean lectin is not a cellular component as has been suggested (*19*). It may instead be localized in the cell walls or apoplastic portion of seed tissues, and its release upon seed hydration may be a result of simple diffusion of the protein from the hydrating apoplasm. This hypothesis is consistent with the recent suggestion (*6*) that, of the lectin activity associated with mung-bean hypocotyl tissue, most is a noncovalently bound component of the cell-wall fraction, and also with the demonstration (*20*) that lectins of cotyledons from jackbean and red kidney bean are localized in clusters of spherical bodies in the intercellular spaces, on the cell walls, and at the periphery of the cytoplasm associated with the cell membrane.

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Aluminum Absorption and Distribution: Effect of Parathyroid Hormone

Abstract. *In rats, gastrointestinal aluminum absorption and tissue distribution were altered by parathyroid hormone; the resultant tissue concentrations were similar to those observed in dialysis patients with a fatal encephalopathy. In dialysis patients, serum aluminum and endogenous parathyroid hormone concentrations are significantly correlated. These data suggest that aluminum toxicity in dialysis patients results from oral aluminum ingestion in the presence of hyperparathyroidism.*

Aluminum has been historically regarded as nonessential (*1*) and nontoxic (*2*). Environmental exposure is virtually universal as aluminum constitutes a substantial part of the earth's crust and is commonly found in food, medicine, and cosmetics. Nevertheless, aluminum toxicity has been observed following the direct application of aluminum salts to cerebral tissues (*3–5*), and there have been increasing reports of aluminum toxicity from environmental exposure. An aluminum ball-mill operator with progressive encephalopathy was found to have brain aluminum concentrations 20 times normal (*6*). High concentrations of aluminum in brain have also been demonstrated in Alzheimer's disease (*3*) and in patients on long-term hemodialysis (*7*). Among these hemodialysis patients was a group with a fatal encephalopathy and brain aluminum concentrations that were 12 times normal. Dialysis patients without encephalopathy had four times the normal concentration of aluminum in the brain.

Patients with dialysis dementia, those with Alzheimer's disease, and the aluminum ball-mill operator all exhibited a progressive encephalopathy characterized by severe motor and behavioral abnormalities. Increased respiratory alumi-

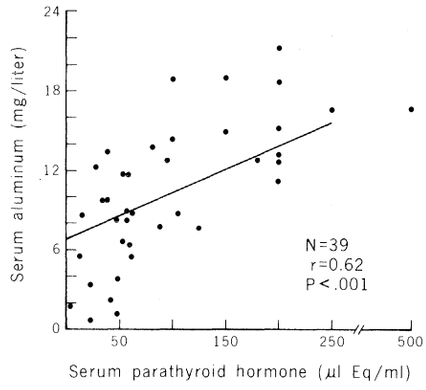

Fig. 1. Relation between serum immunoreactive parathyroid hormone levels and serum aluminum concentrations in dialysis patients.

num exposure was documented in the case of the ball-mill operator. Whether the patients with Alzheimer's disease were exposed to additional aluminum is not clear. However, dialysis patients who are treated with large quantities of aluminum hydroxide phosphate–binding gels have abundant oral exposure to aluminum. These readily available gels are given to dialysis patients to ameliorate phosphate retention (*8*) and are presumably excreted in the feces as insoluble aluminum phosphate. In addition, commercially available aluminum-containing antacids are also commonly used for the treatment of mild gastric upset and ulcers, thereby exposing large populations to potential toxicity. Because of the high parathyroid hormone concentrations seen in dialysis patients (*8, 9*) and the effect of parathyroid hormone on lead absorption and distribution (*10*), we undertook this study to establish a link between gastrointestinal exposure and tissue deposition of aluminum mediated by parathyroid hormone.

Two groups of eight male Sprague-Dawley rats (250 to 300 g) were fed a diet of standard rat chow, ground and supplemented with 0.1 percent aluminum (as aluminum chloride). In addition, group 2 was injected subcutaneously with 17 units of parathyroid hormone extract (TCA-Inolex), twice weekly, in a gelatin base vehicle (84.1 percent water, 15 percent gelatin, 0.1 percent phenol, and 0.8 percent glycerin). Corrected for body weights, the dosages of both aluminum and parathyroid hormone used in the rats are similar to those seen clinically. Serum and whole blood samples were obtained on days 0, 10, and 25. All animals were killed on day 25 and their tissues were removed for analysis. Possible tissue contamination was prevented by removing the gut intact, ligated proximally and distally. Balance data were collected for 6 days (days 6 to 12) by weighing the food and measuring fecal aluminum. In addition, serum aluminum concentrations and serum immunoreactive parathyroid hormone concentrations were determined in 39 long-term hemodialysis patients randomly selected without regard to etiology of kidney disease, oral aluminum intake, or neurologic abnormalities.

Aluminum determinations were made in duplicate on tissue digested with nitric and perchloric acids, using an Instrument Laboratory model 453 atomic emission spectrophotometer at 396 μm. The detection limit of this instrument is 0.01 μg/ml. Replicate determinations agreed within ± 5 percent. White matter determinations represent pooled samples from eight rats, while other determinations were on individual tissue samples. Serum parathyroid hormone concentrations from patients were determined by a sensitive radioimmunoassay, using an antibody raised in chickens against bovine hormone (*11*).

During the 25-day experimental period the control rats consumed 531 mg of aluminum, while those receiving both aluminum and parathyroid hormone consumed 550 mg of aluminum. The balance studies allowed us to interpolate that the 25-day absorption was 7.7 mg higher in the rats treated with parathyroid hormone (70.4 mg) than in the control rats (62.7 mg). Carcass analysis indicated net total body aluminum concentrations of 1.67 mg/kg in the treated rats and 0.47 mg/kg in the control rats. The discrepancy between the absorption and retention of aluminum in these animals suggests renal excretion and is consistent with data on aluminum handling (*12*).

Before treatment (day 0) all animals had appreciable serum and whole blood aluminum concentrations (Table 1). The unsupplemented rat chow was therefore analyzed and an aluminum concentration of 119 mg/kg was found. By day 10, the concentration of aluminum in both serum and whole blood had increased in the control and the treated animals. Serum aluminum in the treated animals was significantly higher ($P < .001$) than in the controls. The concentration of aluminum in whole blood at day 10 for both groups was intermediate between that found in serum and was not different in the two groups. By day 25, the concentrations of serum and whole blood aluminum were similar in both groups, although significantly higher than baseline values ($P < .001$).

Concentrations of aluminum in kidney, muscle, bone, whole brain, and gray matter (Table 2) were significantly higher in the treated animals ($P < .001$). These differences were most marked with respect to whole brain, gray matter, muscle, and bone. The aluminum concentrations in liver and white matter were not different in the two groups. None of the rats displayed overt behavioral changes during the 25 days of observation.

Table 1. Serum and whole blood aluminum concentrations on days 0, 10, and 25 in two groups of male Sprague-Dawley rats receiving dietary aluminum supplementation (group 1) or dietary aluminum supplementation plus parathyroid hormone (group 2). Each value is the mean ± standard deviation for eight rats.

Sample	Aluminum (mg/liter)		
	Day 0	Day 10	Day 25
	Group 1		
Whole blood	0.91 ± 0.01	1.12 ± 0.06	1.09 ± 0.07
Serum	0.85 ± 0.05	1.04 ± 0.07*	1.11 ± 0.05
	Group 2		
Whole blood	0.83 ± 0.06	1.16 ± 0.06	1.15 ± 0.06
Serum	0.91 ± 0.05	1.22 ± 0.08	1.17 ± 0.09

* Significantly different from group 2 ($P < .001$) by Student's *t*-test.

Table 2. Tissue aluminum concentrations on day 25 in two groups of male Sprague-Dawley rats receiving dietary aluminum supplementation (group 1) or dietary aluminum supplementation plus parathyroid hormone (group 2). Each value is the mean ± standard deviation for eight rats, except for the values for white matter, which were determined with pooled samples from eight rats.

Tissue	Aluminum (mg/kg, wet weight)	
	Group 1	Group 2
Whole carcass	0.47 ± 0.03	1.67 ± 0.14*
Bone	2.59 ± 0.29	10.37 ± 0.72*
Kidney	1.31 ± 0.06	2.10 ± 0.11*
Muscle	0.32 ± 0.07	1.63 ± 0.35*
Liver	0.73 ± 0.04	0.71 ± 0.04†
Whole brain	0.74 ± 0.04	2.58 ± 0.15*
Gray matter	0.78 ± 0.05	2.59 ± 0.14*
White matter	0.48	0.55

* Significantly different from group 1 ($P < .001$) by Student's *t*-test. † Not significantly different from group 1 by Student's *t*-test.

Serum immunoreactive parathyroid hormone and aluminum concentrations were determined in the 39 patients who had been on dialysis for 1 to 91 months (Fig. 1). Parathyroid hormone and aluminum concentrations were positively correlated in these patients ($r = .62$, $P < .001$). Gastrointestinal absorption of aluminum hydroxide has been demonstrated among dialysis patients and ranges from 100 to 568 mg/day (*13*). In addition, elevated concentrations of aluminum have been found in the serum of dialysis patients (*12*). These data and those presented here seem to indicate that among dialysis patients exogenous aluminum, in the presence of severely elevated parathyroid hormone, can result in increased gastrointestinal absorption and altered tissue distribution of aluminum.

This conclusion is supported by the high net gastrointestinal absorption demonstrated in rats treated with parathyroid hormone and by the high tissue aluminum concentrations seen in whole brain, gray matter, muscle, bone, and kidney in these animals. These increases, in the absence of increased liver and white matter aluminum, argue against a nonspecific gastrointestinal effect alone and are consistent with a specific effect of parathyroid hormone on both the uptake and the distribution of aluminum in these tissues. The distribution of aluminum in the tissues of these animals is strikingly similar to the distribution of aluminum in dialysis patients who died of a fatal encephalopathy (*7*). The significant correlation of serum parathyroid hormone and aluminum in humans suggests that both Alzheimer's disease and dialysis encephalopathy may be explained in part by parathyroid hormone acting on orally ingested aluminum.

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Competition of Δ^9-Tetrahydrocannabinol with Estrogen in Rat Uterine Estrogen Receptor Binding

Abstract. *Direct competition experiments with Δ^9-tetrahydrocannibinol (Δ^9-THC) and estradiol in binding assays with rat uterine cytosol estrogen receptors showed that Δ^9-THC was a weak, but nevertheless significant, competitor for binding to cytoplasmic estrogen receptors. These data support, at the molecular level, the observations that Δ^9-THC has a weak estrogenic activity (at least the ability to bind to estrogen receptors). Moreover, estrogen-like binding suggests that Δ^9-THC, acting at the level of estrogen receptor, causes a primary estrogenic effect rather than an indirect or secondary phenomenon.*

There has been increasing speculation (*1*) and some experimental support (*2, 3*) for an estrogen-like biological activity associated with heavy, long-term marihuana smoking in man and with the administration of Δ^9-tetrahydrocannabinol (Δ^9-THC) in male rodents. Because most of the data have been obtained from experiments in vivo where specific hormone-sensitive organs were examined for stimulation (*2, 3*) or repression (*4*), the conflicting results may be due to indirect effects in the whole animal.

The reports of uterine stimulation in castrated female rats by Solomon *et al.* (*3*), and of lowered levels of luteinizing hormone, follicle-stimulating hormone, and testosterone in men by Kolodny and co-workers (*2, 5*) after the long-term administration of Δ^9-THC have also focused attention on the estrogenic nature of the drug. Since it has been demonstrated that Δ^9-THC may be transferred across the placenta to the developing fetus (*6*), and that it appears in the milk of lactating animals (*7*), the question of deliterious effects on fetal and newborn offspring must be addressed. Estrogen and estrogenic compounds may play an important part in the development of several forms of carcinoma in human females and their offspring (*8, 9*), and they are potential suppressors of male hormones and of androgen-dependent tissues (*4*). Moreover, it has recently been reported that 4*S* estrogen receptors occur in both human prostate (*10*) and rat testes (*11*).

To test the hypothesis that Δ^9-THC acts as an estrogen in a direct experiment, we have examined the extent to which Δ^9-THC competes with estrogen for sites on rat uterus estrogen receptors in vitro. We have also conducted binding experiments with ^{14}C-labeled Δ^9-THC on rat uterus cytosol to determine the components that can bind Δ^9-THC.

Virgin female (Fisher 344) rats, approximately 60 days old, were decapitated. Their uteri were removed, pulverized in liquid nitrogen, and then homogenized in 10 m*M* tris, 1.5 m*M* EDTA, and 0.5 m*M* dithiothreitol (DTT) at *p*H 7.4 with a Sorvall Omni-Mixer at setting 7 for two 15-second bursts; the suspension was centrifuged at 100,000*g* for 30 minutes at 4°C. The supernatant solution (100 μl; 2 to 4 mg of protein per milliliter) was incubated with increasing amounts of ^{3}H-labeled 17β-estradiol (0.076 to 1.52 pmole; specific activity, 43 c/mmole) for 2 hours at 4°C, and the receptor-bound [^{3}H]estradiol was separated from the free and weakly bound steroid by a 20-minute incubation with dextran-coated charcoal. The charcoal was prepared from a 0.5 percent suspension of Norite A (Sigma) and 0.05 percent dextran (Sigma) in buffer in the usual manner (*12*). The nonspecifically bound [^{3}H]-estradiol not removed by the dextran-coated charcoal was determined by prior incubation (30 minutes) of the uterine cytosol with a 300- to 1000-fold excess of unlabeled 17β-estradiol (556 pmole) relative to ^{3}H-labeled estradiol and measuring the remaining bound estrogen.

The nonspecific binding ranged from about 3 percent of the total bound counts in the case of the lowest levels of labeled estrogen (high ratios of unlabeled to labeled hormone) to a maximum of about 15 percent at the higher levels of labeled