his colleagues, on the other hand, appeared to grow spontaneously and autonomously.

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EFFECT OF POSTURE ON LABORATORY VALUES

To the Editor: A gentle corrective note, if I may, on the excellent article by Tan et al., "Effect of Posture on Serum Lipids," in the August 23 issue of the *Journal*.

In their opening paragraph, the authors say: "In healthy subjects, the plasma volume decreases whereas the concentrations of certain nonfilterable blood constituents increase on change from the recumbent to the upright position, and these alterations are reversed on reversal of the postural positions. *Little account has been taken of such effects in clinical work* [emphasis mine]."

The italicized statement is not precisely correct.

For the last 2½ years, our laboratory has used age, sex, and posture-related normal ranges in reporting results of hospital and office patients. Dr. Russell Hobbie, professor of physics at the University of Minnesota, and I have documented consistent differences in normal ranges between these two groups of patients and have attributed these changes to posture.[1-4]

Our reason for using different sets of normal ranges for the two groups is really quite simple: hospital patients are usually in bed overnight before their blood is drawn in the morning. Therefore, we assign these patients recumbent normal ranges. Office patients, on the other hand, are usually ambulatory and are given upright normal ranges.

To firm up my point, I show in Table 1 the mean of our normal ranges for cholesterol for men in the office and in the hospital.

Table 1. Mean of Normal Range for Cholesterol (SMA-12/60) for Male Office and Male Hospital Patients.

AGE	CHOLESTEROL RANGE		% DIFFERENCE
	MALE OFFICE	MALE HOSPITAL	
yr	*mg/100 ml*		
20	177	157	−11.3
30	201	181	− 9.5
40	216	206	− 9.3
50	222	202	− 9.1
60	220	200	− 9.1
70	210	190	− 9.5
80	200	180	−10.0
90	190	170	−10.5
100	179	159	−11.3

These figures match closely the observation by Tan and his group that cholesterol drops by 10.4 per cent from the upright to the recumbent position. We have also observed postural drops with calcium (-6.8 per cent), total protein (-8.8 per cent), albumin (-6.2 per cent) and protein-bound iodine (-16.3 per cent).[4]

One final point: as a general rule, postural changes seem to increase with age.[4]

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1. Hobbie RK, Reece RL: The use of the computer to suggest diagnostic possibilities from a battery of blood chemistry values. Proceedings of the 1972 San Diego Biomedical Symposium, 1972
2. Reece RL, Hobbie RK: Computer evaluation of chemistry values: a reporting and diagnostic aid. Am J clin Pathol 57:604-615, 1972
3. *Idem:* Letters, notes, and computers: the evolution of a laboratory information system. Conn Med 36:324-332, 1972
4. Reece RL: Position paper. Lufkin Laboratory Letter, November, 1971

NEUROTOXIC EFFECTS OF GLUTAMATE

To the Editor: In a recent article[1] we stated that several animal species are susceptible to the neurotoxic effects of glutamate and related amino acids. In a simultaneously published editorial,[2] Filer and Stegink commented that "the neurotoxic effects of these amino acids in species other than the mouse are debatable." By keeping open the debate, perhaps we can get out the facts on glutamate.

Filer and Stegink invoke "a null effect that may be strain related" as their argument against susceptibility of the rat. We note that the "null effect" referred to was carefully explored by Burde et al.[3,4] and explained in terms of faulty methodology, not strain specificity. In the world literature a dozen separate laboratories[5-15] have reported the rat susceptible to central-nervous-system lesions or associated neuroendocrine and behavioral disturbances from glutamate treatment. Nonrodent species in which neurotoxic effects of glutamate have been reported include rabbit,[16] chick[17] and rhesus monkey.[18,19] We can add abundant unreported data (Olney, J.W., Ho, O.L., Rhee, V., unpublished) further corroborating glutamate-induced brain damage in rabbits, chicks and three strains of rats.

Shifting next to an unstudied species, Filer and Stegink point out that "no neurotoxic effects of glutamate have been reported in the newborn guinea pig. . . ." Some of us (J.O., T.G., V.R.) recently studied guinea pigs because they resemble primates in having a relatively well developed nervous system at birth. We found that the guinea pig, like the primate, is susceptible to glutamate-induced brain damage (Fig. 1*a* and *b*).

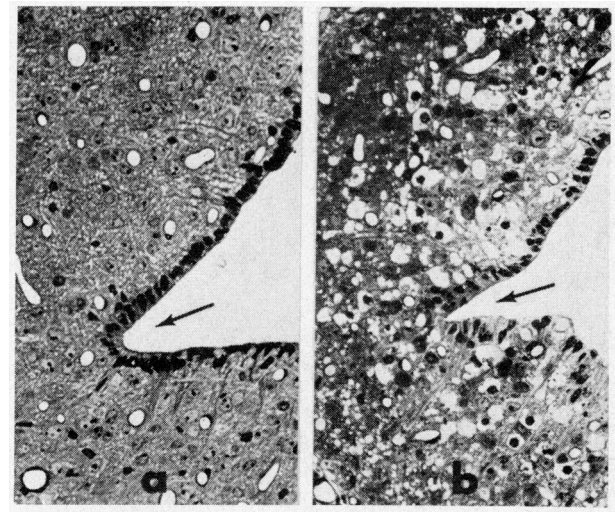

Figure 1. Sections (X200) from Three-Day-Old Guinea-Pig Brains in the Region of Junction (←) of Median Eminence (Bottom) and Arcuate-Periventricular Nucleus of the Hypothalamus (Above).

b, from an animal given sodium glutamate, 1 mg per gram subcutaneously, five hours previously shows numerous necrotic neurons. a, from an animal given sodium chloride, 0.34 mg per gram (molar equivalent to 1 mg per gram of sodium glutamate) five hours previously, appears normal.

Although not denying primate susceptibility, Filer and Stegink are troubled by the way Olney and his colleagues[18,19] describe the glutamate lesion in infant monkeys. They complain that it was initially described as a "massive lesion" resembling "that found in the infant mouse" but later as a "microlesion involving 50 to 90 cells seen only in epon sections." Furthermore, they contend that blood glutamate levels in infant monkeys with "massive" lesions did not differ enough from levels in infants with "micro" lesions to explain the "drastic" descriptive differences. This is not an accurate representation of the reported findings.[18,19] The studies cited[18,19] did include descriptions and illustrations of very large lesions in both mouse and monkey brain. Appropriately, they also included descriptions and illustrations of the opposite extreme — very small lesions involving only a few neurons per section — again, in both mouse and monkey brain. There was no mention of epon sections; in fact, aral-

dite (not epon) was the embedding medium used to illustrate all lesions — large, intermediate and small. The largest lesions in infant monkeys were induced by high subcutaneous doses of glutamate and were accompanied by very high blood glutamate levels (70 to 100 mg per 100 ml); the smallest lesions were induced by low oral doses and were accompanied by relatively low blood glutamate levels (20 mg per 100 ml). For a thoroughly consistent and unambiguous presentation of glutamate neuropathology in infant primates we urge Filer and Stegink to re-examine the cited studies[18,19] carefully.

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1. Olney JW, Ho OL, Rhee V: Brain-damaging potential of protein hydrolysates. N Engl J Med 289:391-395, 1973
2. Filer LJ, Stegink LD: Safety of hydrolysates in parenteral nutrition. N Engl J Med 289:426-427, 1973
3. Burde RM, Schainker B, Kayes J: Acute effect of oral and subcutaneous administration of monosodium glutamate on the arcuate nucleus of the hypothalamus in mice and rats. Nature (Lond) 233:48-60, 1971
4. Burde RM, Schainker B, Kayes J: Monosodium glutamate: necrosis of hypothalamic neurons in infant rats and mice following either oral or subcutaneous administration. J Neuropathol Exp Neurol 31:181, 1972
5. Olney JW: Brain lesions, obesity and other disturbances in mice treated with monosodium glutamate. Science 164:719-721, 1969
6. Arees E, Mayer J: Monosodium glutamate-induced brain lesions: electron microscopic examination. Science 170:549, 1970
7. Everly JL: Light microscopic examination of monosodium glutamate induced lesions in the brain of fetal and neonatal rats. Anat Rec 169:312, 1971
8. Redding TW, Shalley AV, Arimura A, et al: Effect of monosodium glutamate on some endocrine functions. Neuroendocrinology 8:245-250, 1971
9. Knittle JL, Ginsberg-Fellner F: Cellular and metabolic alterations in obese rats treated with monosodium glutamate during the neonatal period. Program and Abstracts of the American Pediatric Society, Atlantic City, New Jersey, April 29, 1970, p 6
10. Bhagavan HN, Coursin DB, Stewart CN: Monosodium glutamate induced convulsive disorders in rats. Nature (Lond) 232:275, 1971
11. Johnston GAR: Convulsions induced in 10-day-old rats by intraperitoneal injection of monosodium glutamate and related excitant amino acids. Biochem Pharmacol 22:137-140, 1973
12. Mushahwar IK, Koeppe RE: The toxicity of monosodium glutamate in young rats. Biochim Biophys Acta 244:318-321, 1971
13. Pradhan SN, Lynch JF: Behavioral changes in adult rats treated with monosodium glutamate in the neonatal stage. Arch Int Pharmacodyn Ther 197:301-302, 1972
14. Weiss LR, et al: Effects of prolonged monosodium glutamate and other high-salt diets on arterial pressure and learning ability in rats. Toxicol Appl Pharmacol 19:389, 1971
15. Hansson HA: Ultrastructure studies on long-term effects of MSG on rat retina. Virchows Arch [Zellpathol] 6:1, 1970
16. Hamatsu T: Effect of soium iodate and sodium L-glutamate on ERG and histological structure of retina of adult rabbits. Nippon Ganka Gakkei Zasshi 68:1621, 1964
17. Snapir, et al: Brain damage in male domestic fowl treated with monosodium glutamate. Poult Sci 50:1511-1514, 1971
18. Olney JW, Sharpe LG: Brain lesions in an infant rhesus monkey treated with monosodium glutamate. Science 166:386-388, 1969
19. Olney JW, Sharpe LG, Feigin RD: Glutamate-induced brain damage in infant primates. J Neuropathol Exp Neurol 31:464-488, 1972

RESERPINE FOR ATHETOSIS

To the Editor: The term extrapyramidal, like other convenient cloaks, presents a false unity concealing the true nature of Parkinsonism, Huntington's chorea, athetosis and tardive dyskinesia. Consequently, this term has suggested therapeutic inferences that may have effects opposite to the desired goal. For example, L-dopa has been administered in athetosis, with, of course, predictable failure.

Some years ago it occurred to me that the motor disorder of Parkinsonism contrasts clinically with athetosis. This idea is supported by neurochemistry and neuropharmacology.

Parkinsonism is now regarded as a syndrome of striatal dopamine depletion, with consequent overbalance of neural activity mediated by acetylcholine transmission,[1] that is aggravated by anticholinesterases traversing the blood-brain barrier. Prolonged administration of reserpine, depleting catecholamine stores, leads to a Parkinsonian-like state. Parkinsonism is improved by antiacetylcholine drugs or replacement of dopamine in the central nervous system by L-dopa.

Although the neurochemical and pharmacologic basis of athetosis has not been pursued with equal zeal as in Parkinsonism, one of the side effects of L-dopa is dyskinetic, choreiform and other adventitious movements. In the 1940's neostigmine received extensive trials without definite benefit, possibly because this quaternary amine does not penetrate the blood-brain barrier.[1] In more recent years, reports on reserpine in phenothiazine-induced dyskinesia and Huntington's chorea indicate improvement.[2-4] Not that we mean to imply a correspondence between these two disorders and athetosis; however, these three states suggest predominance of dopamine and hence stand in contrast to Parkinsonism.

On this basis, we recently tried reserpine on an 18-year-old boy with athetosis associated with hypoxia at birth. He displayed severe grimacing and inco-ordination of all four limbs and axial muscles, without tension, rigidity, increased tendon or stretch reflexes. He had never walked and with difficulty managed his self-care. On 1 mg of reserpine daily for one week, time for brushing teeth was reduced from five minutes and 55 seconds to four minutes and was performed more thoroughly; time for putting on a T-shirt decreased from two minutes and 50 seconds to one minute and 25 seconds, for combing hair, from one minute and 10 seconds to 45 seconds, and for placing standard pegs in holes, from 15 minutes and 11 seconds to 11 minutes and 23 seconds. Grimacing and athetotic movements were less prominent. These results are encouraging and a double-blind study on athetosis is warranted.

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1. Duvoisin RC: Cholinergic-anticholinergic antagonism in Parkinsonism. Arch Neurol 17:124-136, 1967
2. Sato S, Daly R, Peters H: Reserpine therapy in phenothiazine-induced dyskinesia. Dis Nerv Syst 32:680, 1971
3. Duvoisin RC: Reserpine for tardive dyskinesia. N Engl J Med 286:610-611, 1972
4. Kempinski HW, Boniface RW, Morgan PP, et al: Reserpine in Huntington's chorea. Neurology 10:38-42, 1960

STIMULANT DRUGS FOR PROBLEM CHILDREN

To the Editor: In their concise review of the treatment of problem children with stimulant drugs (N Engl J Med 289:407-413, 1973), Sroufe and Stewart condoned the use of such agents in "children whose serious behavior and learning problems are associated with . . . or an ongoing brain dysfunction like epilepsy." We agree that stimulant drugs are exceedingly valuable in the management of these children; however, we should like to call attention to other well defined indications for the use of these medications in epileptic patients, both children and adults.

We reported beneficial results with the use of the amphetamines in the control of epileptic seizures in 1948.[1] At first, we found *dl*-amphetamine sulfate (Benzedrine) to be effective in controlling petit-mal epilepsy in some patients. When the drug was resolved into its two components, *d*-amphetamine (Dexadrine) and *l*-amphetamine, further study established that *d*-amphetamine is of value in the treatment of petit-mal epilepsy, whereas *l*-amphetamine is essentially devoid of anticonvulsant properties. Subsequent use of *d*-amphetamine confirmed its efficacy as an antiepileptic agent.[2-5] Noteworthy is a statement by Goodman and Gilman[6]: ". . . in an occasional child not responding to trimethadione, both the clinical seizures and abnormal EEG discharges may dramatically cease after the administration of amphetamine alone."

In many patients a satisfactory control of seizures can be attained only with dosages of antiepileptic drugs that produce extreme drowsiness. In such cases amphetamine therapy is indicated in an endeavor to alleviate the anticonvulsant-induced drowsiness.

The daily administration of an amphetamine, preferably *d*-am-