Data demonstrating the toxicity of MSG - the human studies

There are few published reports of MSG-induced human adverse reactions. Funding for studies of the safety of MSG comes primarily from the glutamate industry, and only those industry-sponsored studies with negative results (no harm done by MSG) are published.

The first indication that MSG causes adverse reactions was published in 1968 in a letter to the *New England Journal of Medicine (NEJM)* by a physician asking for help in identifying the cause of symptoms that followed dining in a restaurant serving Chinese food.

The first study of MSG-induced brain damage was published in 1969. They were two entirely independent events. The research published in1969 was undertaken by a neuroscientist interested in understanding the brain-damaging potential of glutamic acid. Ultimately, he focused his entire career on study of the brain.

Animal studies demonstrating glutamate-induced brain damage have been discussed in "Data from the 1960s and 1970s demonstrating the toxicity of MSG – the animal studies"

https://www.truthinlabeling.org/Data%20from%20the%201960s%20and%201970s%20d emonstrate_2.html.

Review and critique of animal studies mounted by the glutamate industry to refute the findings of MSG-induced brain damage have been detailed in "The alleged safety of monosodium glutamate (MSG) - The animal studies: A review of the literature and critique of industry sponsored animal research"

https://www.truthinlabeling.org/assets/review_studies.pdf.

By 1980, the toxic effects of monosodium glutamate were so well understood that researchers were using monosodium glutamate as an ablative or provocative tool with which to kill brain cells in laboratory animals. The treated animals would be studied by researchers interested in brain function, or researchers involved in development of pharmaceuticals to treat brain damage, and the fact that monosodium glutamate causes brain lesions and neuroendocrine disorders in laboratory animals became undeniable. Never caught off guard, Ajinomoto acted to draw attention from the toxicity of their product by proclaiming that animal studies do not represent the human condition. In addition, Ajinomoto's International Glutamate Technical Committee (IGTC) began production of human studies that would fail to show a relationship between ingestion of monosodium glutamate and "Chinese restaurant syndrome (CRS)," -- the name assigned to the reactions mentioned in Dr. Robert Ho Man Kwok's 1968 letter to the *NEJM*.

The only reactions that industry acknowledged being caused by ingestion of monosodium glutamate were the few mentioned in the *NEJM* letter, which were said to occur 15-20 minutes after ingestion and last for approximately two hours. And no one

challenged that assertion. Consequently, should a researcher find that subjects in his study expressed fibromyalgia, atrial fibrillation, or went into anaphylactic shock for example following ingestion of MSG, the conclusion of that study would be that there was no evidence of reaction to MSG.

Prior to 1980, glutamate-industry focus had been on refuting the animal studies that demonstrated that MSG caused brain damage. But when that battle appeared to be lost, industry stopped talking about MSG not causing brain damage, and turned to producing **human studies** (often double-blind studies) carefully designed to produce negative results (no harm done by MSG). These studies were then offered to the FDA as proof that MSG was safe. Research protocols used to guarantee their negative results are discussed in "**The alleged safety of monosodium glutamate (MSG)** – **The human studies rigged to produce negative results**"

https://www.truthinlabeling.org/assets/designed_for_deception_short.pdf.

Evidence of MSG-induced human adverse reactions

The 1968 letter to the *NEJM* by Dr. Kwok(175), senior research investigator at the National Biomedical Research Foundation in Silver Spring, Maryland, told colleagues that for several years, since he had been in the United States, he had experienced a strange syndrome whenever he ate in a restaurant serving Northern Chinese food -- an experience he had never experienced in his native land. He reported that 15 or 20 minutes after beginning to eat, he experienced "...numbness at the back of the neck, gradually radiating to both arms and the back, general weakness and palpitation." The syndromes lasted about two hours. He had never heard of such a syndrome until he received complaints of the same symptoms from both medical and nonmedical friends. Through the *NEJM*, he asked his colleagues if they might be interested in seeking more information about this "rather peculiar" phenomenon which someone at the journal dubbed, "Chinese Restaurant Syndrome."

Ten people responded almost immediately. Eight had experienced similar, but not necessarily identical reactions when dining in certain Chinese restaurants (<u>179,180,181,182,183,184,185,186</u>) and, as in Kwok's case, had no clear cut notion of what the causative factor might be. Two had experienced similar reactions which they traced to probable muscarine poisoning(<u>187</u>) or to the potent nonprotein neurotoxin tetrodotoxin, found in the puffer fish(<u>188</u>).

In 1968 Kwok had offered, as one of several hypotheses, that the syndrome might be attributable to the ingestion of "MSG," while a subsequent issue of the *NEJM* carried letters from both Schaumburg and Byck(<u>189</u>) and a group of New York University pharmacology students who had studied the condition for an elective project(<u>190</u>) who stated, unequivocally, that the syndrome which Kwok and his friends had experienced was a reaction to ingesting "MSG."

Schaumburg and Byck(189) pointed out that the reaction being discussed was well known to experienced allergists and Chinese-restaurant owners, and they offered preliminary hypotheses pertaining to the nature of the reaction. Ambos et al.(190) added

that although the reaction had not been cited in the literature, it had been clearly recognized by "...certain persons and within some families." There was general agreement that "MSG" caused a reaction in sensitive individuals which most often consisted of the reactions mentioned by Kwok. Schaumburg and Byck mentioned that syncope, tachycardia, lacrimation, fasciculation and nausea were noticed among the people they had found to be "MSG" sensitive, but all of these were attributed to causes other than MSG. Onset time was 10 to 25 minutes with a duration of 45 minutes to 2 hours. Schaumburg mentioned that 5 grams of "MSG" would produce a reaction in a sensitive individual. Ambos et al.(190) indicated that 2 teaspoons per 6 ounce glass of tomato juice was needed to provoke a reaction in females, while 4 teaspoons per 6 ounce glass was needed to provoke a reaction in males.

In 1969, Schaumburg et al.(<u>191</u>) reported results of studies they had undertaken. This time, both headache and chest pain were added to the symptom list, and a point was made of the fact that there is considerable variability in threshold dose among individuals. Experiments were done with a wide range of test materials and a variety of experimental conditions. Schaumburg et al. concluded "We now have shown that MSG can produce undesirable effects in the amounts used in the preparation of widely consumed foods"(191).

The first article designed to discredit the notion of MSG induced adverse reactions appeared in *Nature* in 1970(<u>195</u>). Morselli and Garattini reported on a study designed to "...assess the significance of subjective reactions." What was meant by "assessing the significance of subjective reactions" was not made clear.

Morselli and Garattini studied both subjective and objective parameters. The 24 subjects were randomly divided into two groups, one group given beef broth with MSG added (the experimental group), the other group (the control group) given beef broth without MSG. All reported subjective symptoms on forms provided. At the same time, blood pressure, pulse, and respiration rate were recorded.

The authors found no statistically significant differences between experimental and control groups in reports of the **symptoms of Chinese Restaurant Syndrome**(CRS) or in objective measures. They reported one female who experienced a panic-like syndrome after being given MSG, "...but it was not associated with any significant modification of objective parameters such as arterial pressure, pulse or respiration rate." And since, "The only subject who described a panic-like syndrome did not experience any burning feeling," the authors conclude that "...MSG administered orally in relatively high doses does not provoke any symptoms of Chinese restaurant syndrome." This, as translated by the food industry, morphed into "MSG is safe."

Noteworthy of the work of Moreslli and Garattini are the following:

1) Objective parameters studied were arterial blood pressure, pulse, and respiration rate. None had ever been shown to be associated with adverse reactions to MSG.

2) Morselli and Garattini discounted the importance of the panic-like syndrome because it is not associated with the objective parameters they had arbitrarily chosen to observe.

3) Subjects were 24 in number, too few to generate statistically significant findings in light of the extreme variability associated with MSG adverse reactions.

4) Seventeen of the 24 subjects were male (believed at the time to be less sensitive to MSG than females(194).

5) Subjects were "healthy volunteers" (never having had any of the symptoms of MSG sensitivity).

6) Subjects were neither randomly selected nor suspected of being MSG sensitive.

Other articles designed to discredit the notion of MSG induced adverse reactions followed. Often results demonstrated MSG toxicity, but in discussion the claim was made that observed reactions were from something other than MSG.

In 1971, a study by Ghadimi et al.(<u>197</u>) focusing on mechanisms which might be relevant to the adverse reactions associated with MSG, demonstrated adverse reactions. They found that the reactions which followed MSG ingestion were "...strikingly similar to those induced by acetylcholine." More important, the discussion does not follow from the results of the study. The authors demonstrated that there were adverse reactions to MSG, but these were not the reactions defined as CRS. The food industry used (and still uses) this as evidence that there is no reaction to MSG.

Following the negative 1970 Morselli and Garattini article(195), came one in 1971 by Rosenblum et al.(<u>198</u>). In the result section of their article, Rosenblum et al. state that using 50 subjects in one of their studies, they found subjects who ingested "MSG" to exhibit significantly more reactions than subjects who had not ingested "MSG." Yet the discussion section states that "...these studies...failed to reveal a single subject who had experienced the triad of symptoms suggestive of the Chinese Restaurant Syndrome." As was often the case, it was the phenomenon of CRS, not the phenomenon of MSG sensitivity, that was studied. The food industry used (and still uses) this as evidence that there is no reaction to MSG.

In 1972, Upton and Barrows(<u>192</u>) warned that, based on their observations of an epileptic woman, it would seem reasonable to advise patients on diphenylhydantoin to avoid foods rich in "MSG."

The next study was one done in 1972 by Kenney and Tidball(15). They reported that "Thirty-two percent of the persons tested responded at the 5-g level when challenged by a single placebo-controlled exposure [to MSG]." They also suggested that "It seems likely that monosodium L-glutamate taken as the salt is not physiologically equivalent to glutamic acid ingested in protein."

It is of interest to note that after the 1972 report, Kenney began to turn out studies as needed for The Glutamate Association. In a 1979 paper, Kenney(<u>199</u>) quotes from his

earlier work, provides evidence from two studies which demonstrate human adverse reactions to MSG, has a "however" in the discussion and conclusions, which relates to some percentage figures for MSG levels (that defy interpretation), and finally suggests that what might appear to be a reaction to MSG can be explained away as an esophageal reaction.

A variety of human studies and comments on human adverse reactions were published between 1973 and 1978.

Reif-Lehrer's first article appeared in 1975(200) as correspondence in the *NEJM*. She wrote that children react to MSG ingestion, and described symptoms similar to adults with almost the same degree of prevalence. She presented three cases and discussed the relation between shudder in children, epileptic "seizures", "MSG shivers", and the fact the MSG has been reported to cause convulsive disorders in animals. Subsequently, Andermann, et al. commented on a possible relationship between MSG and essential tremor(201).

During the next two years, Reif-Lehrer published an additional report of children's apparent adverse reactions to MSG(202); results of a questionnaire study establishing that 25% of those responding to the questionnaire, and 30% of the persons reporting that they had been exposed to Chinese restaurant food, reported adverse reactions (203); and a lengthy review and report on the possible significance of adverse reactions to MSG in humans (174). In the last report, published in 1976, Reif-Lehrer raised the question of whether particular groups of individuals might be adversely affected by eating unregulated amounts of MSG.

Colman(204) wrote to the *NEJM* in 1978, reporting two cases of psychiatric reactions to MSG.

From time to time, case reports were published describing instances of adverse reactions associated with ingestion of MSG. There are reports of tachycardia(<u>213</u>), hyperactive or hysterical activity in children(<u>214,215</u>), paraesthesiae of hands and feet(<u>216</u>), severe "burning" headache(<u>217</u>), severe upper abdominal pain and pressure accompanied by diaphoresis and a burning sensation in the chest(217), angio-oedema(<u>218</u>), and a hypertensive reaction(<u>219</u>) in the form of vascular headache typical of those seen in patients taking monoamine oxidase inhibitors. Ratner et al.(217) reported that the initial diagnoses in seven patients whose complaints were eventually resolved as MSG sensitivity were migraine (twice), myocardial infarction, brain tumor, neurosis, functional colitis, and depression.

Comments and observations also have been published. In 1976, Neumann(220) reported having seen reactions involving frequent ventricular premature beats. He cautioned that, "Because sensitivity to MSG is not rare and because of the unpredictable consequences given a damaged, vulnerable, or irritable myocardium, patients with a tendency to rhythm disturbances should be made wary of prefabricated soups, and meat 'tenderizers,' in addition to the fare of Chinese restaurants. Incidentally, the term 'Chinese restaurant syndrome,' while picturesque, is too narrow

considering the tons of MSG used in less exotic foods. The syndrome should really be termed what it is, an MSG atopy. And the cardiovascular system is its chief target" (220).

In 1980, Gore and Salmon(221) observed 55 subjects given randomized MSG and placebo trials, and noted that although the reactions to MSG were significant, the symptoms recorded were not those of the CRS. They questioned the meaning of reaction to symptoms which were not CRS. Sauber(222) pointed out that the meaning was perfectly clear -- that the symptoms which Gore and Salmon found to be most prevalent, were, indeed, the most prevalent visible effects of MSG.

Asthma was studied extensively by Allen who published in 1981 and 1987(<u>223,224</u>). He explored and discussed the possible relation of MSG to asthma, questioning the possible links, and exploring possible mechanisms for a relationship. In a single blind study using 32 subjects with asthma, some of whom had histories of severe asthma after Chinese restaurant or similar meals, he found a dose dependent reaction which in some cases was delayed up to 12 hours.

Moneret-Vautrin(<u>225</u>) reported finding a "...very small subset of patients with intrinsic asthma..." with an intolerance to high doses (2.5g) of MSG.

Studies that discuss the toxic effects of MSG are not done in the United States. Industry will not fund them, medical journals will not publish them, American media will not discuss them, and in cases that are important to the glutamate industry, those who report adverse reactions will be denigrated (237).

An excellent example of this last point is the work of David Allen, M.D, which was of the utmost importance to the glutamate industry. The glutamate-industry plan was to establish the claim that it took 3 grams or more MSG to trigger a reaction, even though few, if any, products actually contained 3 grams or more MSG. Then if pressure to clearly label products that contained MSG became problematic for the industry, they would assert that only MSG in products that contained 3 grams or more MSG in processed foods would go unlabeled.

Allen, a physician in private practice in Australia, had found that 3 grams of MSG could trigger asthma, and had published his research in a peer reviewed journal. That research would be cited by the glutamate industry as demonstration of the fact that 3 grams of MSG could cause an adverse reaction -- without mention of the fact that evidence that 3 grams of MSG triggers adverse reactions is in no way evidence that amounts *less* than 3 grams wouldn't do the same. But industry had a problem with using Allen's data, for Allen had also found that .5 grams of MSG could trigger asthma. And if that information surfaced, it could kill the 3-gram scheme.

The plan to establish 3 grams as the cutting point for identifying MSG in processed food was set in motion years ago in anticipation that there might be renewed pressure on the FDA to warn of the dangers of MSG. It beautifully illustrates the skill of the glutamate

industry in manipulating fact, and the strong bonds between government and industry. How the glutamate industry handled this possibility is covered in the book, *It Wasn't Alzheimer's, It Was MSG*(237).

Although no researcher in the United States today dares to suggest MSG might be toxic, there are researchers outside of the United States who have warned of the dangers of ingesting MSG. The file **"Researchers warning that manufactured free glutamate in food might contribute to adverse events"**

https://www.truthinlabeling.org/assets/researchers_warnings.pdf offers that information.

Possibly more telling of the toxicity of MSG and its excitotoxic manufactured free glutamate component (MfG) are the MSG-safety studies done (and rigged to produce negative results) under the direction of IGTC chairman Andrew Ebert, Ph.D., (Ajinomoto's agent in charge of research at the time). Those studies were aimed at convincing the medical community as well as the public that MfG, along with MSG, are harmless.

There is a significant body of such literature proclaiming the safety of MSG. Cleverly contrived to conclude (not prove) that MSG is harmless, it involved a variety of researchers from various universities and medical schools, all given study protocols and supervised by Ebert. Although they had common elements, no two studies were identical. There was, however, one element that was shared by all -- the use of placebos that would cause reactions identical to those caused by MSG.

These studies lay the foundation for industry propaganda wherein the claim is made that the toxicity of MSG has never been demonstrated, and, therefore, MSG is harmless. They are discussed in "The *alleged* safety of monosodium glutamate (MSG) – The human studies rigged to produce negative results. https://www.truthinlabeling.org/assets/designed_for_deception_short.pdf

REFERENCES

1. This paper may be reproduced fully and distributed in that form without permission of the author. However, **no portions** of this paper may be reproduced or transmitted in any form or by any means, electronic, mechanical, or other, without permission in writing from the author: <u>questionsaboutMSG@gmail.com</u>

2. Kizer, J.S., Nemeroff, C.B., and Youngblood, W.W. Neurotoxic amino acids and structurally related analogs. <u>Pharmacological Reviews</u> 29: (4) 301-318, 1978.

3. <u>Van Nostrand's Scientific Encyclopedia</u>, 6th Edition, (1983.) s.v. "Flavor enhancers and potentiators." pp 1211-1212.

4. Schwartz, G. R. In Bad Taste: The MSG SyndromeSanta Fe: Health Press, 1988, pp 7-10.

5. Flavor and Acceptability of Monosodium Glutamate. Proceedings of the Symposium. <u>The First Symposium on Monosodium Glutamate</u> The Quartermaster Food and container Institute for the Armed Forces, and Associates, Food and container Institute, Chicago, March 4, 1948.

6. Shank, P. and Aprison, M.H. Glutamate as a neurotransmitter, In <u>Glutamine and</u> <u>Glutamate in Mammals</u>, Vol 2, Dramine, E., Ed., Boca Raton: CRC Press, 1988.

7. Garattini, S. Evaluation of the neurotoxic effects of glutamic acid. In: <u>Nutrition and the</u> <u>Brain</u> Vol 4, Wurtman, R.J. Ed. New York: Raven Press, 1979.

8. 7. <u>Frontiers in Excitatory Amino Acid Research Neurology and Neurobiology</u> Vol 46, Cavalheiro, E.A., Lehmann, J., and Turski, L., Eds., New York: Liss, 1988.

9. Freedland, R.A., and Briggs, S. <u>A Biochemical Approach to Nutrition</u> New York: Halsted Press, 1977.

10. Zim, H.S. Your Stomach and Digestive Tract New York: William Morrow, 1973.

11. Burgess, J. <u>How our Bodies Work: Food and Digestion</u> Englewood Cliffs: Silver Burdett, 1988.

12. Prendergast, K. Protein hydrolysate - a review. Food Trade Review 44: 14-20, 1974.

13. Ward, B.R. <u>The Human Body: Food and Digestion</u> New York: Franklin Watts, 1982.

14. Lynch, J.F., Jr., Lewis, L.M., and Adkins, J.S. (**Division of Nutrition, FDA, Washington, D.C. 20204**). Monosodium glutamate-induced hyperglycemia in weanling rats. <u>J S Fed Proc</u> 31: 1477, 1971.

15. Kenney, R.A. and Tidball, C.S. Human susceptibility to oral monosodium Lglutamate. <u>Am J Clin Nutr</u> 25:140-146, 1972.

16. Code of Federal Regulations Food and Drugs 21: Parts 100-169, 1990.

17. Code of Federal Regulations Food and Drugs 21: Parts 170-199, 1989.

18. Quotes signify terminology used as defined by the FDA.

19. Olney, J.W., Ho, O.L., and Rhee, V. Brain-damaging potential of protein hydrolysates. <u>N Engl J Med</u> 289: 391-393, 1973.

20. Schainker, B., and Olney, J.W. Glutamate-type hypothalamic-pituitary syndrome in mice treated with aspartate or cysteate in infancy. <u>J Neural Transmission</u> 35: 207-215, 1974.

21. Weinberg, G.H. and Schumaker, J.A. <u>Statistics: An Intuitive Approach</u> Belmont: Wadsworth, 1962.

22. McNemar, Q. Psychological StatisticsNew York: Wiley, 1949.

23. Ferguson, G.A. <u>Statistical Analysis in Psychology and Education</u> New York: McGraw-Hill, 1959.

24. Evaluation of certain food additives and contaminants. Thirty-first report of the Joint FAO/WHO Expert Committee on Food Additives. <u>World Health Organization Technical</u> <u>Report Series 759</u> Geneva: World Health Organization, 1987.

25. L-glutamic acid and its ammonium, calcium, monosodium and potassium salts.<u>WHO</u> Food Additive Series: 22. Toxicological Evaluation of Certain Food Additives. Prepared by the 31st Meeting of the Joint FAO/WHO Expert Committee on Food Additives. International Programme on Chemical Safety. 1987 pp. 97-143.

26. Lucas, D.R. and Newhouse, J. P. The toxic effect of sodium-L-glutamate on the inner layers of the retina. <u>AMA Arch Ophthalmol</u> 58: 193-201, 1957.

27. Himwich, H.E., Wolff, K., Hunsicker, A.L. and Himwich, W.A. Some behavioral effects associated with feeding sodium glutamate to patients with psychiatric disorders. <u>J Nerv & Mental Disease</u> 121: 40-49, 1955.

28. Astin, A.W., and Ross, S. Glutamic Acid and human intelligence. <u>Psychological</u> <u>Bulletin</u> 57:429-434, 1960.

29. <u>Nutrition Reviews</u> Monosodium glutamate-studies on its possible effects on the central nervous system. 28: 124-129, 1970.

30. Albert, K, Hoch, P., and Waelsch, H. Preliminary report on the effect of glutamic acid administration in mentally retarded subjects. <u>J Nerv and Ment Disease</u> 104: 263-274, 1946.

31. Zimmerman, F.T., Burgemeister, H.B. and Putnam, T.J. Effect of glutamic acid on the intelligence of patients with mongolism. <u>Arch Neurol & Psychiat</u> 61: 275-287, 1949.

32. Milliken, J.R. and Standen, J.L. An investigation into the effects of glutamic acid on human intelligence. <u>J Neurol Neurosurg Psychiat</u> 14: 47-54, 1951.

33. Gasster, M. Clinical experience with L-glutavite in aged patients with behavior problems and memory defects. <u>J Am Geriatrics Society</u> 9: 370-375, 1961.

34. Unna, K. and Howe, E.E. Toxic effects of glutamic and aspartic acid. <u>Fed Proc</u> 4: 138, 1945.

35. Madden, S.C., Woods, R.R., Skull, F.W. Remington, J.H., and Whipple, G.H. Tolerance to amino acid mixtures and casein digests given intravenously. <u>J Exp Med</u> 81: 439-448, 1945.

36. Levey, S., Harroun, J.E. and Smyth, C.J. Serum glutamic acid levels and the occurrence of nausea and vomiting after intravenous administration of amino acid mixtures. J Lab Clin Med 34: 1238-1248, 1949.

37. Elman, R. The intravenous use of protein and protein hydrolysates. <u>Ann New York</u> <u>Acad Sc</u> 47: 345-357, 1946.

38. Mayer-Gross, W. and Walker, J.W. The effect of L-glutamic acid and other aminoacids in hypoglycemia, <u>Biochem J</u> 44: 92-97, 1949.

39. Weil-Malherbe, H. The action of glutamic acid in hypoglycaemic coma. <u>J Ment Sc</u> 95: 930-944, 1949.

40. Goodman, L.S., Swinyard, E.A., and Toman J.E.P. Effects of L-glutamic acid and other agents on experimental seizures. <u>Arch Neurol & Psychiat</u> 56: 20-29, 1946.

41. Waelsch, H., and Price, J.C. Biochemical aspects of glutamic acid therapy for epilepsy. <u>Arch Neurol Psychiat</u> 51: 393, 1944.

42. Price, J.C., Waelsch, H., and Putnam, T.J. DL-glutamic acid hydrochloride in treatment of petit mal and psychomotor seizure. <u>J Am Med Assoc</u> 122: 1153-1156, 1943.

43. Pond, E.A., and Pond, M.H. Glutamic acid and its salts in petit mal epilepsy. <u>J</u> <u>Mental Sci</u> 97: 663, 1951.

44. Walshe, J.M. The effect of glutamic acid on the coma of hepatic failure. <u>Lancet</u> 1: 1075, 1953.

45. Alexander, R.W., Berman, E, and Balfour, D.C. Jr. Relationship of glutamic acid and blood ammonia to hepatic coma. <u>Gastroenterology</u> 29: 711-718, 1955.

46. Fincle, L.P., and Reyna, L.J. A one year study of L-Glutavite on long term hospitalized, elderly, schizophrenic patients. <u>J Clin Exp Psychopath</u> 19: 7-18, 1958.

47. Himwich, W.A. Absorption of I-glutamic acid. Science 120: 351-352, 1954.

48. Zimmerman, F.T., Burgmeister, B.B., and Putnam, T.J. The ceiling effect of glutamic acid upon intelligence in children and in adolescence. <u>Amer J Psychiat</u> 104: 593-599, 1948.

49. Potts, A.M., Modrell, R.W., and Kingsbury, C. Permanent fractionation of the electroretinogram by sodium glutamate. <u>Am J Ophthalmol</u> 50: 900-907, 1960.

50. Freedman, J.K., and Potts, A.M. Repression of glutaminase I in the rat retina by administration of sodium L-glutamate. <u>Invest Ophthalmol</u> 1: 118-121, 1962.

51. Freedman, J.K., and Potts, A.M. Repression of glutaminase I in rat retina by administration of sodium L-glutamate. <u>Invest Ophthal</u> 2: 252, 1963.

52. Potts, A.M. Selective action of chemical agents on individual retinal layers. In: <u>Biochemistry of the retina</u>. Graymore, C.N., Ed. New York: Academic Press, 1965. pp 155-161.

53. Hamatsu, T. Experimental studies on the effect of sodium iodate and sodium Lglutamate on ERG and histological structure of retina in adult rabbits. <u>Acta Soc</u> <u>Ophthalmol Jpn</u> 68: 1621-1636, 1964. (Abstract)

54. Hansson, H.A. Ultrastructure studies on long-term effects of MSG on rat retina. <u>Virchows Arch [Zellpathol]</u> 6: 1, 1970.

55. Cohen, A.I. An electron microscopic study of the modification by monosodium glutamate of the retinas of normal and "rodless" mice. <u>Am J Anat</u> 120: 319-356, 1967.

56. Olney, J.W. Glutamate-induced retinal degeneration in neonatal mice. Electronmicroscopy of the acutely evolving lesion. <u>J Neuropathol Exp Neurol</u> 28: 455-474, 1969.

57. Hansson, H.A. Scanning electron microscopic studies on the long term effects of sodium glutamate on the rat retina. <u>Virchows Arch ABT B (Zellpathol)</u> 4: 357-367, 1970.

58. Arees, E., Sandrew, B., and Mayer, J. MSG-induced optic pathway lesions in infant mice following subcutaneous injection. <u>Fed Proc</u> 30: 521, 1971.

59. Olney, J.W. Brain lesions, obesity, and other disturbances in mice treated with monosodium glutamate. <u>Science</u> 164: 719-721, 1969.

60. Olney, J.W. Ho, O.L., and Rhee, V. Cytotoxic effects of acidic and sulphur containing amino acids on the infant mouse central nervous system. <u>Exp Brain Res</u> 14: 61-76, 1971.

61. Olney, J.W., and Sharpe, L.G. Brain lesions in an infant rhesus monkey treated with monosodium glutamate. <u>Science</u> 166: 386-388, 1969.

62. Snapir, N., Robinzon, B., and Perek, M. Brain damage in the male domestic fowl treated with monosodium glutamate. <u>Poult Sci</u> 50: 1511-1514, 1971.

63. Perez, V.J. and Olney, J.W. Accumulation of glutamic acid in the arcuate nucleus of the hypothalamus of the infant mouse following subcutaneous administration of monosodium glutamate. <u>J Neurochem</u> 19: 1777-1782, 1972.

64. Arees, E.A., and Mayer, J. Monosodium glutamate-nduced brain lesions: electron microscopic examination. <u>Science</u> 170: 549-550, 1970.

65. Arees, E.A., and Mayer, J. Monosodium glutamate-induced brain lesions in mice. Presented at the 47th Annual Meeting of American Association of Neuropathologists, Puerto Rico, June 25-27, 1971. <u>J Neuropath Exp Neurol</u> 31: 181, 1972. (Abstract)

66. Everly, J.L. Light microscopy examination of monosodium glutamate induced lesions in the brain of fetal and neonatal rats. <u>Anat Rec</u> 169: 312, 1971.

67. Olney, J.W. Glutamate-induced neuronal necrosis in the infant mouse hypothalamus. <u>J Neuropathol Exp Neurol</u> 30: 75-90, 1971.

68. Lamperti, A., and Blaha, G. The effects of neonatally-administered monosodium glutamate on the reproductive system of adult hamsters. <u>Biol Reprod</u> 14: 362-369, 1976.

69. Takasaki, Y. Studies on brain lesion by administration of monosodium L-glutamate to mice. I. Brain lesions in infant mice caused by administration of monosodium L-glutamate. <u>Toxicology</u> 9: 293-305, 1978.

70. Holzwarth-McBride, M.A., Hurst, E.M., and Knigge, K.M. Monosodium glutamate induced lesions of the arcuate nucleus. I. Endocrine deficiency and ultrastructure of the median eminence. <u>Anat Rec</u> 186: 185-196, 1976.

71. Holzwarth-McBride, M.A., Sladek, J.R., and Knigge, K.M. Monosodium glutamate induced lesions of the arcuate nucleus. II Fluorescence histochemistry of catecholamines. <u>Anat Rec</u> 186: 197-205, 1976.

72. Paull, W.K., and Lechan, R. The median eminence of mice with a MSG induced arcuate lesion. <u>Anat Rec</u> 180: 436, 1974.

73. Burde, R.M., Schainker, B., and Kayes, J. Acute effect of oral and subcutaneous administration of monosodium glutamate on the arcuate nucleus of the hypothalamus in mice and rats. <u>Nature</u>(Lond) 233: 58-60, 1971.

74. Olney, J.W. Sharpe, L.G., Feigin, R.D. Glutamate-induced brain damage in infant primates. <u>J Neuropathol Exp Neurol</u> 31: 464-488, 1972.

75. Abraham, R., Doughtery, W., Goldberg, L., and Coulston, F. The response of the hypothalamus to high doses of monosodium glutamate in mice and monkeys: cytochemistry and ultrastructural study of lysosomal changes. <u>Exp Mol Pathol</u> 15: 43-60, 1971.

76. Burde, R.M., Schainker, B., and Kayes, J. Monosodium glutamate: necrosis of hypothalamic neurons in infant rats and mice following either oral or subcutaneous administration. <u>J Neuropathol Exp Neurol</u> 31: 181, 1972.

77. Robinzon, B., Snapir, N., and Perek, M. Age dependent sensitivity to monosodium glutamate inducing brain damage in the chicken. <u>Poult Sci</u> 53: 1539-1942, 1974.

78. Tafelski, T.J. Effects of monosodium glutamate on the neuroendocrine axis of the hamster. <u>Anat Rec</u> 184: 543-544, 1976.

79. Coulston, F. In: Report of NAS,NRC, Food Protection Subcommittee on Monosodium Glutamate. July, 1970. pp 24-25.

80. Inouye, M. and Murakami, U. Brain lesions and obesity in mouse offspring caused by maternal administration of monosodium glutamate during pregnancy. <u>Congenital Anomalies</u> 14: 77-83, 1974.

81. Olney, J.W., Rhee, V. and DeGubareff, T. Neurotoxic effects of glutamate on mouse area postrema. <u>Brain Research</u> 120: 151-157, 1977.

82. Olney, J.W., Ho, O.L. Brain damage in infant mice following oral intake of glutamate, aspartate or cystine. <u>Nature</u>(Lond) 227: 609-611, 1970.

83. Lemkey-Johnston, N., and Reynolds, W.A. Incidence and extent of brain lesions in mice following ingestion of monosodium glutamate (MSG). <u>Anat Rec</u> 172: 354, 1972.

84. Takasaki, Y. Protective effect of mono- and disaccharides on glutamate-induced brain damage in mice. <u>Toxicol Lett</u> 4: 205-210, 1979.

85. Takasaki, Y. Protective effect of arginine, leucine, and preinjection of insulin on glutamate neurotoxicity in mice. <u>Toxicol Lett</u> 5: 39-44, 1980.

86. Lemkey-Johnston, N., and Reynolds, W.A. Nature and extent of brain lesions in mice related to ingestion of monosodium glutamate: a light and electron microscope study. <u>J Neuropath Exp Neurol</u> 33: 74-97, 1974.

87. Olney, J. W. Brain damage and oral intake of certain amino acids. In: <u>Transport</u> <u>Phenomena in the Nervous System: Physiological and Pathological Aspects</u> Levi, G., Battistin, L., and Lajtha, A. Eds. New York: Plenum Press, 1976.

88. Reynolds, W.A., Lemkey-Johnston, N., Filer, L.J. Jr., and Pitkin, R.M. Monosodium glutamate: absence of hypothalamic lesions after ingestion by newborn primates. <u>Science</u> 172: 1342-1344, 1971.

89. Matsuyama, S. Studies on experimental obesity in mice treated with MSG. <u>Jap J Vet</u> <u>Sci</u> 32: 206, 1970.

90. Redding, T.W., Schally, A.V., Arimura, A., and Wakabayashi, I. Effect of monosodium glutamate on some endocrine functions. <u>Neuroendocrinology</u> 8: 245-255, 1971.

91. Knittle, J.L., Ginsberg-Fellner, F. Cellular and metabolic alterations in obese rats treated with monosodium glutamate during the neonatal period. <u>Program and Abstracts</u> of the American Pediatric Society Atlantic City, New Jersey, April 29, 1970, p6. or <u>Bulletin Am Peds Soc Gen Mtg Program Abstracts</u> p 6, April 1970.

92. Araujo, P.E., and Mayer J. Activity increase associated with obesity induced by monosodium glutamate in mice. <u>Am J Physiol</u> 225: 764-765, 1973.

93. Nagasawa, H., Yanai R., and Kikuyama, S. Irreversible inhibition of pituitary prolactin and growth hormone secretion and of mammary gland development in mice by monosodium glutamate administered neonatally. <u>Acta Endocrinol</u> 75: 249-259, 1974.

94. Nemeroff, C.B., Grant, L.D., Bissette, G., Ervin, G.N., Harrell, L.E., and Prange, A.J., Jr. Growth, endocrinological and behavioral deficits after monosodium L-glutamate in the neonatal rat: Possible involvement of arcuate dopamine neuron damage. <u>Psychoneuroendocrinology</u> 2: 179-196, 1977.

95. Nemeroff, C.B., Konkol, R.J., Bissette, G., Youngblood, W., Martin, J.B., Brazeau, P., Rone, M.S., Prange, A.J. Jr., Breese, G.R. and Kizer, J.S. Analysis of the disruption in hypothalamic-pituitary regulation in rats treated neonatally with monosodium glutamate (MSG): Evidence for the involvement of tuberoinfundibular cholinergic and dopaminergic systems in neuroendocrine regulation. <u>Endocrinology</u> 101: 613-622, 1977.

96. Pizzi, W.J., Barnhart, J.E., and Fanslow, D.J. Monosodium glutamate administration to the newborn reduces reproductive ability in female and male mice. <u>Science</u> 196: 452-454, 1977.

97. Tafelski, T.J. and Lamperti, A.A. The effects of a single injection of monosodium glutamate on the reproductive neuroendocrine axis of the female hamster. <u>Biol Reprod</u> 17: 404-411, 1977.

98. Takasaki, Y, Sekine, S., Matsuzawa, Y., Iwata, S., and Sasaoka, M. Effects of parenteral and oral administration of monosodium L-glutamate (MSG) on somatic growth in rats. <u>Toxicol Lett</u> 4: 327-343, 1979.

99. Matsuzawa, Y., Yonetani, S., Takasaki, Y., Iwata, S., and Sekine, S. Studies on reproductive endocrine function in rats treated with monosodium L-glutamate early in life. <u>Toxicol Lett</u> 4: 359-371, 1979.

100. Matsuyama, S., Oki,Y., and Yokoki, Y. Obesity induced by monosodium glutamate in mice. <u>Natl Inst Anim Health Q</u>(Tokyo) 13: 91-101, 1973.

101. Pizzi, W.J., and Barnhart, J.E. Effects of monosodium glutamate on somatic development, obesity and activity in the mouse. <u>Pharmacol Biochem Behav</u> 5: 551-557, 1976.

102. Nikoletseas, M.M. Obesity in exercising, hypophagic rats treated with monosodium glutamate. <u>Physiol Behav</u> 19: 767-773, 1977.

103. Redding, T.W., and Schally, A.V. Effect of monosodium glutamate on the endocrine axis in rats. <u>Fed Proc Fed Am Soc Exp Biol</u> 29: 378A (abstract #755), 1970.

104. Holzwarth, M.A., and Hurst, E.M. Manifestations of monosodium glutamate (MSG) induced lesions of the arcuate nucleus of the mouse. <u>Anat Rec</u> 178: 378, 1974.

105. Trentini, G.P., Botticelli, A., and Botticelli, C.S. Effect of monosodium glutamate on the endocrine glands and on the reproductive function of the rat. <u>Fertil Steril</u> 25: 478-483, 1974.

106. Lynch, J.F. Jr., Lewis, L.M., Hove, E.L., and Adkins, J.S. **Division of Nutrition**, **FDA**, **Washington**, **D.C. 20204.**Effect of monosodium L-glutamate on development and reproduction in rats.<u>Fed Proc</u> 29: 567Abs, 1970.

107. Pradhan, S.N., Lynch, J.F., Jr. Behavioral changes in adult rats treated with monosodium glutamate in the neonatal state. <u>Arch Int Pharmacodyn Ther</u> 197: 301-304, 1972.

108. Iwata, S., Ichimura, M., Matsuzawa, Y., Takasaki, Y., and Sasaoka, M. Behavioral studies in rats treated with monosodium L-glutamate during the early states of life. <u>Toxicol Lett</u> 4: 345-357, 1979.

109. Vorhees, C.V., Butcher, R.E., Brunner, R.L., and Sobotka, T.J. A developmental test batter for neurobehavioral toxicity in rats: a preliminary analysis using monosodium glutamate, calcium carrageenan, and hydroxyurea. <u>Toxicol Appl Pharm</u> 50: 267-282, 1979.

110. Vogel, J.R., and Nathan, B.A. Learned taste aversions induced by high doses of monosodium L-glutamate. <u>Pharmacol Biochem Behav</u> 3: 935-937, 1975.

111. Berry, H.K., and Butcher, R.E. Biochemical and behavioral effects of administration of monosodium glutamate to the young rat. <u>Soc Neurosci</u> 3rd Ann Mtg. S.D. 5/8/1973.

112. Berry, H.K., Butcher, R.E., Elliot, L.A., and Brunner, R.L. The effect of monosodium glutamate on the early biochemical and behavioral development of the rat. <u>Devl</u> <u>Psychobiol</u> 7: 165-173, 1974.

113. Weiss, L.R., Reilly, J.F., Williams, J., and Krop, S. Effects of prolonged monosodium glutamate and other high salt diets on arterial pressure and learning ability in rats. <u>Toxicol Appl Pharmacol</u> 19: 389, 1971.

114. Bhagavan, H.N., Coursin, D.B., and Stewart, C.N. Monosodium glutamate induces convulsive disorders in rats. <u>Nature</u>(London) 232: 275-276, 1971.

115. Johnston, G.A.R. Convulsions induced in 10-day-old rats by intraperitoneal injection of monosodium glutamate and related excitant amino acids. <u>Biochem</u> <u>Pharmacol</u> 22: 137-140, 1973.

116. Mushahwar, I.K. and Koeppe, R.E. The toxicity of monosodium glutamate in young rats. <u>Biochem Biophys Acta</u> 244: 318-321, 1971.

117. Nemeroff, C.B., and Crisley, F.D. Lack of protection by pyridoxine or hydrazine pretreatment against monosodium glutamate induced seizures. <u>Pharmacol Biochem</u> <u>Behav</u> 3: 927-929, 1975.

118. Nemeroff, C.B., and Crisley, F.D. Monosodium L-glutamate induced convulsions: temporary alteration in blood-brain barrier permeability to plasma proteins. <u>Environ</u> <u>Physiol Biochem</u> 5: 389-395, 1975.

119. Wiechert, P. Gollinitz, G. Metabolic investigations of epileptic seizures: the activity of the glutamate decarboxylase prior to and during experimentally produced convulsions. <u>J Neurochem</u> 15: 1265-1270, 1968. (Abstract)

120. Wiechert, P., and Herbst, A. Provocation of cerebral seizures by derangement of the natural balance between glutamic acid and y-aminobutyric acid. <u>J Neurochem</u> 13: 59-64, 1966.

121. Wiechert, P., and Gollnitz, G. Metabolic investigations of epileptic seizures: investigations of glutamate metabolism in regions of the dog brain in preconvulsive states. <u>J Neurochem</u> 17: 137-147, 1970. (Abstract)

122. Olney, J.W. and Price, M.T. Neuroendocrine interactions of excitatory and inhibitory amino acids. <u>Brain Research Bulletin</u> 5: Suppl 2, 361-368, 1980.

123. Olney, J.W. and Price M.T. Excitotoxic amino acids as neuroendocrine probes. In: <u>Kainic Acid as a Tool in Neurobiology</u>McGeer, E.G., et al. Eds. New York: Raven Press, 1978.

124. Olney, J.W. Excitotoxic amino acids: research applications and safety implications. In: <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> Filer, L.J. Jr., et al. Ed. New York: Raven Press, 1979.

125. Nemeroff, C.B. Monosodium glutamate-induced neurotoxicity: review of the literature and call for further research. In: <u>Nutrition & Behavior</u> Miller, S.A., Ed. Philadelphia: The Franklin Institute Press, 1981.

126. Although "seemingly logical," <u>data</u> suggest that glutamate is metabolized by humans quite differently than it is metabolized by the monkey; and that, in fact, human metabolism of glutamate more closely resembles that of the mouse. (See Reference 168)

127. Olney, J.W., Labruyere, J., and DeGubareff, T. Brain damage in mice from voluntary ingestion of glutamate and aspartate. <u>Neurobehav Toxicol</u> 2: 125-129, 1980.

128. Olney, J.W., Cicero, T.J., Meyer, E.R., and DeGubareff, T. Acute glutamatenduced elevations in serum testosterone and luteinizing hormone. <u>Brain Research</u> 112: 420-424, 1976. 129. The arcuate nucleus is an area of the hypothalamus which has been shown to sustain considerable damage from GLU administration.

130. Toth, L., Karcsu, S., Feledi, J., and Kreutzberg, G.W. Neurotoxicity of monosodium-L-glutamate in pregnant and fetal rats. <u>Acta Neuropathologica</u> 75: 16-22, 1987.

131. Adamo. N.J., and Ratner, A. Monosodium glutamate: Lack of effects on brain and reproductive function in rats. <u>Science</u> 169: 673-674, 1970.

132. Oser, B.L., Carson, S., Vogin, E.E., and Cox, G.E. Oral and subcutaneous administration of monosodium glutamate to infant rodents and dogs. <u>Nature</u> 229: 411-413, 1971.

133. Olney, J.W. Monosodium glutamate effects. Science 172: 294, 1971.

134. Olney, J.W. Toxic effects of glutamate and related amino acids on the developing central nervous system. In:<u>Heritable Disorders of Amino Acid Metabolism</u> Nyhan, W.L. Ed. New York: Wiley, 1974. pp 501-512.

135. Murakami, U., Inouye, M. Brain lesions in the mouse fetus caused by maternal administration of monosodium glutamate. <u>Congenital Anomalies</u> 11: 161- 171-177, 1971.

136. Filer, L.J., and Stegink, L.D. Safety of hydrolysates in parenteral nutrition. <u>N Engl J</u> <u>Med</u> 289: 426-427, 1973.

137. Olney, J.W., Ho, O.L., Rhee, V., and DeGubareff, T. Neurotoxic effects of glutamate. <u>New Engl J. Med</u> 289: 1374-1375, 1973.

138. Lowe, C.U. Monosodium glutamate: specific brain lesion questioned. <u>Science</u>167: 1016, 1970.

139. Zavon, M.R., Monosodium glutamate: specific brain lesion questioned. <u>Science</u>167: 1017, 1970.

140. Olney, J.W., and Sharpe, L.G. Monosodium glutamate: specific brain lesion questioned. <u>Science</u> 167:1017, 1970.

141. Blood, F.R., Oser, B.L. and White, P.L. Monosodium glutamate. <u>Science</u> 165:1028-1029, 1969.

142. Olney, J.W. Monosodium glutamate. Science 165: 1029, 1969.

143. Reynolds, W.A., Lemkey-Johnston, N., Filer, L. J. Jr., and Pitkin, R.M. Monosodium Glutamate: absence of hypothalamic lesions after ingestion by newborn primates. <u>J Neuropath Exp Neurol</u> 31: 181-182, 1972. (Abstract)

144. Reynolds, W.A., Lemkey-Johnston, N., Filer, L. J., Jr. and Pitkin, R.M. Monosodium glutamate: absence of hypothalamic lesions after ingestion by newborn primates. Paper presented and discussed at 47th Annual Meeting, Amer. Assoc. Neuropath., Puerto Rico, June, 1971.

145. Abraham, R., Swart, J., Goldberg, L., and Coulston, F. Electron microscopic observations of hypothalami in neonatal rhesus monkeys (Macaca mulatta) after administration of monosodium L-glutamate. Exp Mol Pathol 23: 203-213, 1975.

146. Newman, A.J., Heywood, R., Palmer, A.K., Barry, D.H., Edwards, F.P., and Worden, A.N. The administration of monosodium L-glutamate to neonatal and pregnant rhesus monkeys. <u>Toxicology</u> 1: 197-204, 1973.

147. Stegink, L.D., Reynolds, W.A., Filer, L.J. Jr., Pitkin, R.M., Boaz, D.P., and Brummel, M.C. Monosodium glutamate metabolism in the neonatal monkey. <u>Am J</u> <u>Physiol</u> 229: 246-250, 1975.

148. Reynolds, W.A., Butler, V., Lemkey-Johnston, N. Hypothalamic morphology following ingestion of aspartame or MSG in the neonatal rodent and primate: a preliminary report. <u>J Toxicol environmental Health</u> 2: 471-480, 1976.

149. Heywood, R., and Worden, A.N. Glutamate Toxicity in Laboratory Animals. In: <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> Filer, L.J. Jr., et al. Ed. New York: Raven Press, 1979. pp 203-215.

150. Ebert, A.G. Chronic toxicity and teratology studies of monosodium L-glutamate and related compounds. <u>Toxicol Appl Pharmacol</u> 17: 274, 1970.

151. Owen, G., Cherry, C.P., Prentice, D.E., and Worden, A.N. The feeding of diets containing up to 4% monosodium glutamate to rats for 2 years. <u>Toxicol Lett</u> 1: 221-226, 1978.

152. Owen, G., Cherry, C.P., Prentice, D.E. and Worden, A.N. The feeding of diets containing up to 10% monosodium glutamate to Beagle dogs for 2 years. <u>Toxicol Lett</u>1: 217-219, 1978.

153. Semprini, M.E., D'Amicis, A., and Mariani, A. Effect of monosodium glutamate on fetus and newborn mouse. <u>Nutr Metabol</u> 16: 276-284, 1974.

154. Wen, C.P., Hayes, K.C., and Gershoff, S.N. Effects of dietary supplementation of monosodium glutamate on infant monkeys, weaning rats, and suckling mice. <u>Am J Clin Nutr</u> 26: 803-813, 1973.

155. Ebert, A.G. The Dietary administration of monosodium glutamate or glutamic acid to C-57 black mice for two years. <u>Toxicol Lett</u> 3: 65-70, 1979.

156. Ebert, A.G. The dietary administration of L-monosodium glutamate, DLmonosodium glutamate and L-glutamic acid to rats. <u>Toxicology Letters</u> 71-78, 1979. 157. Anantharaman, K. <u>In utero</u> and dietary administration of monosodium L-glutamate to mice: reproductive performance and development in a multigeneration study. In: <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> New York: Raven, 1979, pp 231-253.

158. Huang, P.C., Lee, N.Y., Wu, T.J., Yu, S.L., and Tung, T.C. Effect of monosodium glutamate supplementation to low protein diets on rats. <u>Nutr Rep Intern</u> 13: 477-486, 1976.

159. Takasaki, Y. Studies on brain lesions after administration of monosodium Lglutamate to mice. II Absence of brain damage following administration of monosodium L-glutamate in the diet. <u>Toxicology</u> 9: 307-318, 1978.

160. Bunyan, J., Murrell, E.A., and Shah, P.P. The induction of obesity in rodents by means of monosodium glutamate. <u>Br J Nutr</u> 35: 25-29, 1976.

161. Rippere, V. Placebo-controlled tests of chemical food additives: are they valid? <u>Medical Hypotheses</u> 7: 819-823, 1981.

162. Goldschmiedt, M., Redfern, J.S., and Feldman, M. Food coloring and monosodium glutamate: effects on the cephalic phase of gastric acid secretion and gastrin release in humans. <u>Am J Clin Nutr</u> 51: 794-797, 1990.

163. Heywood, R., James, R.W., and Worden, A.N. The ad libitum feeding of monosodium glutamate to weanling mice. <u>Toxicol Lett</u> 1: 151-155, 1977.

164. Takasaki, Y., Matsuzawa, Y., Iwata, S., O'Hara, Y., Yonetani, S., and Ichimura, M. Toxicological studies of monosodium L-glutamate in rodents: relationship between routes of administration and neurotoxicity. In: <u>Glutamic Acid: Advances in Biochemistry</u> <u>and Physiology</u>Filer, L.J. Jr., Garattini, S., Kare, M.R., Reynolds, W.A., and Wurtman, R.J. Eds. New York: Raven Press, 1979.

165. Semprini, M.E., Conti, L., Ciofi-Luzzatto, A. and Mariani, A. Effect of oral administration of monosodium glutamate (MSG) on the hypothalamic arcuate region of rat and mouse: a histological assay. <u>Biomedicine</u> 21: 398-403, 1974.

166. Prabhu, V.G., and Oester, Y.T. Neuromuscular functions of mature mice following neonatal monosodium glutamate. <u>Arch Int Pharmacodyn</u> 189: 59-71, 1971.

167. Lengvari, I. Effect of perinatal monosodium glutamate treatment on endocrine functions of rats in maturity. <u>Acta Biol Acad Sci Hung</u> 28: 133-141, 1977.

168. Perez, V.J. and Olney, J.W. Accumulation of glutamic acid in the arcuate nucleus of the hypothalamus of the infant mouse following subcutaneous administration of monosodium glutamate. <u>J Neurochem</u> 19: 1777-1782, 1972.

169. Stegink, L.D., Pitkin, R.M., Reynolds, W.A., Filer, L.J., Boaz, D.P., and Brummel, M. Placental transfer of glutamate and its metabolites in the primate. <u>Am J Obstetrics</u> <u>Gynecology</u> 122: 70-78, 1975.

170. Pitkin, R.M., Reynolds, W.A., Stegink, L.D., and Flier, L.J. Jr. Glutamate Metabolism and Placental Transfer in Pregnancy.<u>Glutamic Acid. Advances in</u> <u>Biochemistry and Physiology</u> Filer, L.J., Jr. et al., Eds. New York: Raven Press, 1979.

171. Olney, J.W. and Price, M.T. Neuroendocrine effects of excitotoxic amino acids. In: <u>Glutamate as a Neurotransmitter.</u> DiChiara, G., and Gessa, G. L. Eds., New York: Raven, 1981, pp.423-432.

172. Olney, J.W. Excitatory neurotoxins as food additives: an evaluation of risk. <u>Neurotoxicology</u> 2: 163-192, 1980.

173. General Aviation News July 31, 1989 page 6.

174. Reif-Lehrer, L. Possible significance of adverse reactions to glutamate in humans. <u>Federation Proceedings</u> 35: 2205-2211, 1976.

175. Kwok, R.H.M. The Chinese restaurant syndrome. Letter to the editor. <u>N Engl J</u> <u>Med</u> 278: 796, 1968.

176. Zorumski, C.F. Environmental excitotoxins and neurodegenerative disorders. <u>Biol</u> <u>Psychiatry</u> 27: 90A, 1990.

177. Hosen, H. Correspondence Re: Airway Effects of MSG. <u>J Asthma</u> 25: (2) 111-112, 1988.

178. Nichaman, M.A. and McPherson, R.S. Estimating prevalence of adverse reactions to foods: principles and constraints. <u>J Allergy Clin Immunol</u> 78: 148-154, 1986.

179. Schaumburg, H. Chinese-restaurant Syndrome. <u>N Engl J Med</u> 278: 1122, 1968.

180. McCaghren, T.J. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

181. Menken, M. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278, 1123, 1968.

182. Migden, W. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

183. Rath, J. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

184. Beron, E.L. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

185. Kandall, S.R. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

186. Gordon, M.E., Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123-1124, 1968.

187. Rose, E.K. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1123, 1968.

188. Davies, N.E. Chinese-restaurant syndrome. <u>N Engl J Med</u> 278: 1124, 1968.

189. Schaumburg, H.H. and Byck, R. Sin cib-syn: accent on glutamate. <u>N Engl J</u> <u>Med</u>279: 105, 1968.

190. Ambos, M., Leavitt, N.R., Marmorek, L., and Wolschina, S.B. Sin cib-syn: accent on glutamate. <u>N Engl J Med</u> 279: 105, 1968.

191. Schaumburg, H.H., Byck, R., Gerstl, R., and Mashman, J.H. Monosodium Lglutamate: its pharmacology and role in the Chinese restaurant syndrome. <u>Science</u> 163: 826-828, 1969.

192. Upton, A.R.M., and Barrows, H.S. Chinese-restaurant syndrome recurrence. <u>N</u> Engl J Med 286: 893-894, 1972

193. There is mention, in a number of the responses to Dr. Kwok's 1968 letter, that the adverse reactions were not a new phenomenon, but had been experienced for some years prior to 1968.

194. Himms-Hagen, J. Correspondence: Chinese restaurant syndrome. <u>Nature</u> 228: 97, 1970.

195. Morselli, P., and Garattini, S. Monosodium-glutamate and the Chinese restaurant syndrome. <u>Nature</u> (London) 227:611-612, 1970.

196. Bazzano, H., D'Elia, J.A., Olson, R.E. Monosodium glutamate: feeding of large amounts in man and gerbils. <u>Science</u>169: 1208-1209, 1970.

197. Ghadimi, H., Kumar, S., and Abaci, F. Studies on monosodium glutamate ingestion: 1. biochemical explanation of Chinese Restaurant Syndrome. <u>Biochemical Medicine</u> 5: 447-456, 1971.

198. Rosenblum, I., Bradley, J.D., and Coulston, F. Single and double blind studies with oral monosodium glutamate in man. <u>Toxicology and Applied Pharmacology</u> 18: 367-373, 1971.

199. Kenney, R.A. Placebo-controlled studies of human reaction to oral monosodium Lglutamate. In: <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> Filer, L.J. Jr., et al., Eds. New York: Raven Press, 1979.

200. Reif-Lehrer, L. and Stemmermann, M.B. Correspondence: Monosodium glutamate intolerance in children. <u>N Engl J Med</u> 293: 1204-1205, 1975.

201. Andermann, F., Vanasse, M., and Wolfe, L.S. Correspondence: Shuddering attacks in children: essential tremor and monosodium glutamate. <u>N Engl J Med</u> 295: 174, 1975.

202. Reif-Lehrer, L. Letter: A search for children with possible MSG intolerance. <u>Pediatrics</u> 58: 771-772, 1976.

203. Reif-Lehrer, L. A questionnaire study of the prevalence of chinese restaurant syndrome. <u>Fed Proc</u> 36:1617-1623, 1977.

204. Colman, A.D. Possible psychiatric reactions to monosodium glutamate. <u>N Engl J</u> <u>Med</u> 299: 902, 1978.

205. Kenney, R.A. Possible psychiatric reactions to monosodium glutamate. <u>N Engl J</u> <u>Med</u> 300: 503, 1979.

206. Colman, A.D. Possible psychiatric reactions to monosodium glutamate. <u>N Engl J</u> <u>Med</u> 300: 503, 1979.

207. Kenney, R.A. The Chinese restaurant syndrome: an anecdote revisited. <u>Fd Chem</u> <u>Toxic</u> 24: 351-354, 1986.

208. Kerr, G.R., Wu-Lee, M., El-Lozy, M., McGandy, R., and Stare, F. Foodsymptomatology questionnaires: risks of demand-bias questions and population-biased surveys. In: <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> Filer, L. J., et al., Eds. New York: Raven Press, 1979.

209. Wilkin, J.K. Does monosodium glutamate cause flushing (or merely "glutamania")? <u>J Am Acad Dermatology</u> 15: 225-230, 1986.

210. Kerr, G.R., Wu-Lee, M., El-Lozy, M., McGandy, R., and Stare, F.J. Objectivity of food-symptomatology surveys. <u>J Am Diet Assoc</u> 71: 263-268, 1977.

211. Stegink, L.D., Filer, L.J. Jr., Baker, G.L., and Bell, E.F. Plasma glutamate concentrations in 1-year-old infants and adults ingesting monosodium L-glutamate in consomme. <u>Pediatric Research</u>20: 53-58, 1986.

212. Stegink, L.D., Reynolds, W.A., Filer, L.J., Jr., Baker, G.L., Daabees, T.T., and Pitkin, R.M. Comparative metabolism of glutamate in the mouse, monkey, and man. <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> Filer, L.J., Jr. et al. Eds. New York: Raven Press, 1979.

213. Gann, D. Ventricular tachycardia in a patient with the "Chinese restaurant syndrome." <u>Southern Medical J</u> 70: 879-880, 1977.

214. Asnes, R.S. Chinese restaurant syndrome in an infant. <u>Clin Pediat</u> 19: 705-706, 1980.

215. Cochran, J.W., and Cochran A.H. Monosodium glutamania: the Chinese restaurant syndrome revisited. <u>JAMA</u> 252: 899, 1984.

216. Freed, D.L.J. and Carter, R. Neuropathy due to monosodium glutamate intolerance. <u>Annals of Allergy</u> 48: 96-97, 1982.

217. Ratner, D., Esmel, E., and Shoshani, E. Adverse effects of monosodium glutamate: a diagnostic problem. <u>Israel J Med Sci</u> 20: 252-253, 1984.

218. Squire, E.N. Jr. Angio-oedema and monosodium glutamate. Lancet 988, 1987.

219. Pohl, R., Balon, R., and Berchou, R. Reaction t chicken nuggets in a patient taking an MAOI. <u>Am J Psychiatry</u> 145: 651, 1988.

220. Neumann, H.H. Soup? It may be hazardous to your health. <u>Am Heart J</u> 92:, 266, 1976.

221. Gore, M.E., and Salmon, P.R. Chinese restaurant syndrome: fact or fiction. <u>Lancet</u> 1(8162): 251, 1980.

222. Sauber, W.J. What is Chinese restaurant syndrome? <u>Lancet</u> 1(8170): 721-722, 1980.

223. Allen, D.J., and Baker, G.J. Chinese-restaurant asthma. <u>N Engl J Med</u> 305: 1154-1155, 1981.

224. Allen, D.H., Delohery, J., & Baker, G.J. Monosodium L-glutamate-induced asthma. Journal of Allergy and Clinical Immunology 80: No 4, 530-537, 1987.

225. Moneret-Vautrin, D.A. Monosodium glutamate-induced asthma: Study of the potential risk in 30 asthmatics and review of the literature. <u>Allergic et Immunologie</u> 19: No 1, 29-35, 1987.

226. Schwartzstein, R.M., Kelleher, M., Weinberger, S.E., Weiss, J.W., & Drazen, J.M. Airway effects of monosodium glutamate in subjects with chronic stable asthma. <u>Journal of Asthma</u> 24: No 3, 167-172, 1987.

227. Weisse, A.B. On Chinese restaurants, prolapsing heart valves, and other medical conundrums. <u>Hospital Practice</u> 275-282, 1989.

228. Filer, L.J., Jr., Garattini, S., Kare, M.R., Reynolds, W.A. and Wurtman, R.J. Eds. <u>Glutamic Acid: Advances in Biochemistry and Physiology</u> New York: Raven Press, 1979.

229. Olney, J.W. Excitatory amino acids and neuropsychiatric disorders. <u>Biol</u> <u>Psychiatry</u> 26: 505-525, 1989.

230. Choi, D.W., and Rothman. S.M. The role of glutamate neurotoxicity in hypoxicischemic neuronal death. <u>Annu Rev Neurosci</u> 13: 171-182, 1990. 231. Olney, J.W. Excitotoxic amino acids and neuropsychiatric disorders. <u>Annu Rev</u> <u>Pharmacol Toxicol</u> 30: 47-71, 1990.

232. Olney, J.W. Excitotoxicity: an overview. Biol Psychiatry 27: 90A, 1990. (Abstract)

233. Coyle, J.T. Glutamate receptors and age-related neurodegenerative disorders. <u>Biol</u> <u>Psychiatry</u> 27: 91A, 1990.

234. Pomara, N., Deptula, D., Singh, R., LeWitt, P.A., and Banay-Schwartz, M. Excitatory amino acid concentrations in CSF of patients with Alzheimer's disease. <u>Biol</u> <u>Psychiatry</u> 27: 91A, 1990.

235. Zukin, S.R., and Javitt, D.C. The NMDA-PCP theory of schizophrenia: implications of receptor interactions. <u>Biol Psychiatry</u> 27: 91A, 1990.

236. Olney, J.W. Excitotoxins and neurological diseases. Proceedings of the 11th International Congress of Neuropathology, Kyoto, Japan, September 2-8, 1990. (in press)

237. Samuels, A. It Wasn't Alzheimer's. It Was MSG. Chapter 6, p.77 and Chapter 9, p 104. Self-published. August, 2013.