

## BIRTH ORDER IN PROGENIES OF CHEMICAL WARFARE-INTOXICATED IRANIAN PEOPLE

ALI AKBAR MOSHTAGHIE, M.D., AND HAMID POUR-JAFARI, M.S.

*From the School of Medicine, Hamadan University of Medical Sciences, P.O. Box 518, Hamadan,  
Islamic Republic of Iran.*

### ABSTRACT

In the present work we studied the birth order in progenies of Iranian survivors of Iraqi chemical attacks during a period from 1984 to 1989. Then we compared the results with the birth order of the control group. Despite a slight difference between the birth order in the two groups of progenies, this was not statistically significant. This does not mean, however, that there are no genetic consequences due to war chemicals. A number of autosomal recessive mutants may have been produced but they will not become manifest for several generations.

*MJIRI, Vol. 9, No. 2, 111-112, 1995.*

### INTRODUCTION

Although chemical and biological weapons are banned by the 1925 Geneva protocol and the 1927 Convention on Biological Weapons, they have been used in both military zones and also against civilian populated areas at the Iran-Iraq border. There are numerous reports providing evidence on their use in different parts of the world.<sup>1,2,3</sup>

Respiratory and hematological complications are potentially fatal, and could be long-lasting. Although many of the victims of these savage attacks have been discharged, long-term follow-up is required in order to assess the morbidity and even mortality rates.<sup>4</sup> Alteration in libido is another problem in gassed men.<sup>5</sup>

Perhaps worst of all are their teratogenic<sup>6</sup> and mutagenic<sup>7</sup> actions. Unfortunately, human research in this area is not easily available. In order to perform human genotoxicological investigations, it is necessary to study congenital malformations, sex ratio, fetal deaths<sup>8</sup>, and the birth order in progenies of these victims. In the present work we investigated the birth order in progenies of intoxicated Iranian people. We did not find any references in our review study; but there were some studies concerning birth order in the offspring of irradiated people.

### MATERIAL AND METHODS

In this study the subjects were progenies of a randomly selected population of survivors of Iraqi chemical attacks. A

total of 802 married men aged 18-85 ( $\bar{x} = 33.5$ ) years were interviewed. About one fourth of them (25.4%) expressed that their wives (aged 15 to 63,  $\bar{x} = 29.00$  years) had also been exposed. 387 (48.0%) were civilian, 237 (29.7%) revolutionary guards, 151 (18.9%) volunteer forces and 27 (3.4%) military personnel. It was impossible for us to determine whether the same gases had been used, as no analysis was performed on our samples. There was no doubt, however, that they were injured with chemical war agents, and their names were on the list of chemical victims in official reports. The victims reported that the chemical agent most frequently used by Iraqi forces in their chemical attacks was mustard gas.

Our subjects had between 0 and 14 children. In the analysis, their progenies were distributed into two groups; group I, who were born before intoxication of one or both parents (control group) and group II who were born after parental exposure. Then, the birth order in these two groups were statistically compared.

### RESULTS AND DISCUSSION

The results of our study are summarized in Table I. Column II, row 3, states the total number of first children (569) who were born before their parents' exposure, and row 2 states the number of male births (335) in this group of progenies. Column II, row 6 states the total number of first children who were born after their parents' exposure (137), and row 5 states the number of male births (79) in this group.

Column II, rows 4 and 7 show the male/total birth ratio of

## Birth Order in Progenies of Chemical Warfare Victims

Table I. Birth order of 1st to > 6th child among two groups; group I: control group, and group II: progenies of intoxicated victims who were born after parental exposure. It also shows the results of statistical comparison.

Column I		Column II	Column III	Column IV	Column V	Column VI	Column VII	Column VIII
Birth order		1st Child	2nd Child	3rd Child	4th Child	5th Child	6th Child	>6th Child
GROUP I	No. of male births	335	230	164	109	64	34	22
	Total no. of male and female births	569	429	303	205	115	61	46
	Male/total birth ratio	0.588752	0.536131	0.541254	0.531707	0.556522	0.557377	0.478261
GROUP II	No. of male births	79	63	55	44	26	20	15
	Total no. of male and female births	137	108	99	78	51	38	36
	Male/total birth ratio	0.576642	0.583333	0.555556	0.564103	0.509804	0.526316	0.416667
Rate ratio		1.021	0.919081	0.974257	0.942572	1.09164	1.05902	1.14783
Z-test		0.166171	0.593573	0.167377	0.331177	0.377134	0.203507	0.412068
P-value		0.868018	0.552795	0.867068	0.740507	0.706071	0.838734	0.680286

progenies, and finally row 10 of column III presents the same information on 2nd children and so on. As P-values (row 10 of columns II to VIII) show, there are no significant differences between the birth order among progenies who were born before and after their parents' intoxication with war gases. In other words, this investigation showed that chemical warfare agents have no detectable effect on the birth order of progenies of victims.

Despite this result, we have to take into account the parental aging factor in group II, and therefore question whether group I was a suitable control group or not. Some reports<sup>9</sup> have shown that parental aging affects birth order and increases female births. Therefore, the results of this study may actually show that war chemicals affect birth order by way of decreasing the number of female births. Another unpublished report<sup>10</sup> which showed that parental exposure to chemical war gases may increase the secondary sex ratio, may strengthen this hypothesis that parental exposure to war chemicals may have an effect on the birth order of progenies.

### ACKNOWLEDGEMENT

The authors wish to thank Mr. Mahjob, M.S. and our students for their help and assistance.

### REFERENCES

1. Crocker GB: The evidence of chemical and toxin weapon use in Southeast Asia and Afghanistan. Proceedings of the First

World Congress, New Compounds in Biological and Chemical Warfare: Toxicological Evaluation, Ghent, Belgium, May 21-23, pp. 384-412, 1984.

- Heyndrickx A, Heyndrickx B: Comparison of toxicological investigations in man in southeast Asia, Afghanistan and Iran. Proceedings of the First World Congress, New Compounds in Biological and Chemical Warfare: Toxicological Evaluation, Ghent, Belgium, May 21-23, pp. 426-434, 1984.
- Bahadori FM, Shakoobi A: Autopsy finding on Iranian victims of chemical warfare. Article No. 31, Abstracts of the First International Medical Congress on Chemical Warfare Agents in Iran, Mashhad Univ., June 13-16, 1988.
- Sohrabpour H: Clinical manifestations of chemical agents on Iranian combatants during the Iran-Iraq conflict. Proceedings, First World Congress, New Compounds in Biological and Chemical Warfare: Toxicological Evaluation, Ghent, Belgium, May 21-23, pp. 291-297, 1984.
- Pour-Jafari H, Moshtaghi AA: Alterations of libido in gassed Iranian men. Vet Hum Toxicology 34 (6): 547, 1992.
- Hassanzadeh FM, et al: A literature review on the teratogenic action of sulfur mustard and an experimental work of its effects on mouse embryopathy. Abstracts of the First International Medical Congress on Chemical Warfare Agents in Iran, Mashhad Univ., June 13-16, Article No 47, 1988.
- Auerbach C: Forty years of mutation research: a pilgrim's progress. Heredity 40: 177-187, 1978.
- Pour-Jafari H: Fetal deaths and parental exposure to chemical warfare agents. Med J Islam Rep Iran 6 (2): 87-88, 1992.
- Moran PAP, Novitski E, Novitski C: Parental age and the secondary sex ratio. Ann Hum Genet 32: 315-316, 1969.
- Pour-Jafari H: Secondary sex ratio in progenies of Iranian intoxicated victims. Veterinary and Human Toxicology (In Press).

## CLINICAL CORRELATIONS BETWEEN AUDITORY BRAINSTEM RESPONSE AND MAGNETIC RESONANCE IMAGING IN PATIENTS WITH DEFINITE MULTIPLE SCLEROSIS

MASOOD KAVIANI, M.D., ABDUL-HOSSEIN JAFARY\*, Ph.D., AND  
ALI-ASGHAR PEYVANDI, M.D.

*From the E.N.T. Department and the\* Department of Audiology, Shiraz University of Medical Sciences,  
Shiraz, Islamic Republic of Iran.*

### ABSTRACT

In an attempt to assess objectively the integrity of the auditory pathways in 30 patients with definite multiple sclerosis (MS), an audiometric evaluation was performed and auditory brainstem responses (ABRs) were obtained.

Stressing the auditory system by increasing the stimulation rate showed some enhancement in the identification of MS. 24 (80%) patients had an abnormal ABR along with clinical signs of brainstem dysfunction at the time of assessment by magnetic resonance imaging (MRI), while those without such signs had no incidence of abnormalities. This is independent of the clinical classification of the patients.

*MJIRI, Vol. 9, No. 2, 113-116, 1995.*

### INTRODUCTION

The auditory behaviour of patients suffering from MS has been extensively studied during the past three decades.<sup>1,7</sup> Although auditory complaints are rarely the initial symptoms of the disease, appropriate functional tests may detect acoustic abnormalities, often subtle in the majority of the patients. Noffsinger et al.<sup>8</sup> found abnormal audiologic findings in the majority of cases, but only 7.0% of his 61 patients had auditory symptoms initially.

The development of electrical response audiometry and especially the application of the noninvasive technique of Sohmer and Feinmesser<sup>5,9</sup> opened new vistas in the study of MS. Although the diagnosis of MS depends primarily on clinical criteria, electrophysiological techniques have an important role in demonstrating lesions that are clinically silent, thereby helping to establish multiple lesions in patients with clinical evidence of an abnormality at only one site.

More recently, MRI has revealed multiple central nervous system abnormalities in patients with clinically definite MS.<sup>2,3,12,13,14</sup> By demonstrating lesions at several sites in the

neuraxis, MRI may also be an important means of establishing the diagnosis of MS in patients presenting clinically with only a single lesion.

We have compared the diagnostic utility of MRI and ABR in patients with MS.

To accomplish this, we have only studied patients with clinically definite MS<sup>6</sup> which had been previously confirmed by MRI and who had brainstem involvement in the majority of cases.

### MATERIAL AND METHODS

A total of 30 patients with MS confirmed by MRI were referred by neurologists for otolaryngeal and audiological evaluation. The ages of the patients ranged from 17 to 45 years (average 30.8 years). The study group consisted of 15 males and 15 females with disease durations of 1 month to 120 months from the onset of MS (with a mean of 35.6 months).

Each patient underwent a pertinent history, an ear and



## Correlations Between ABR & MRI in MS

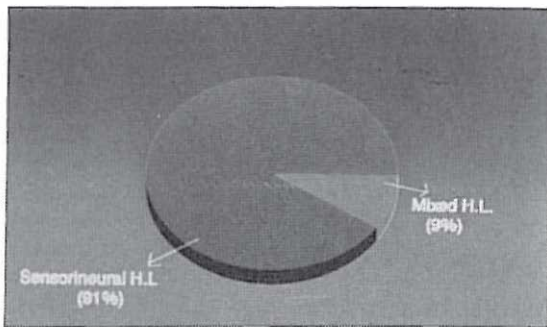


Fig. 1. Sensorineural and mixed hearing loss percentages.

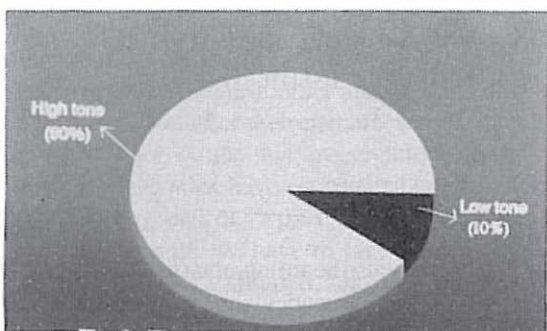
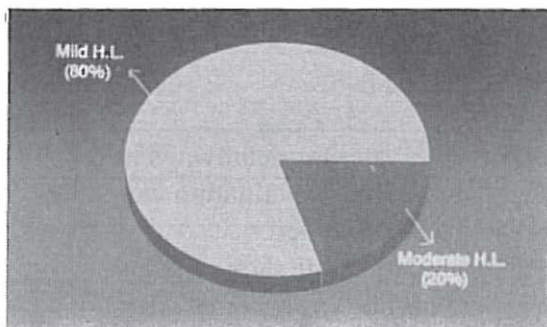


Fig. 2. The type and degree of hearing loss.

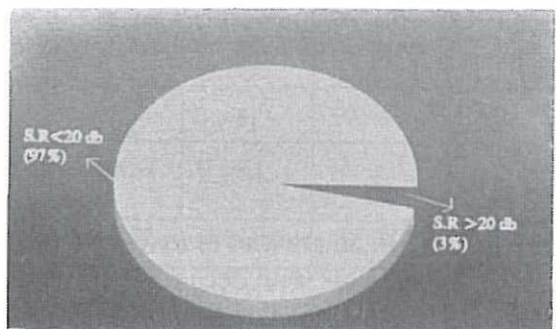
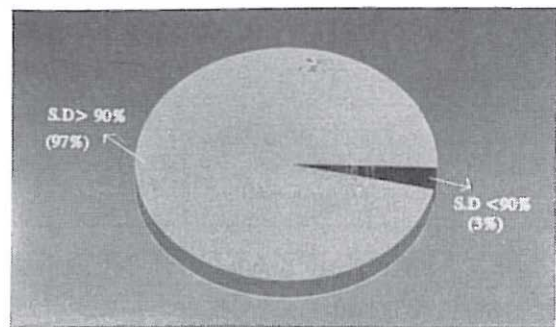


Fig. 3. Speech reception and discrimination percentages.

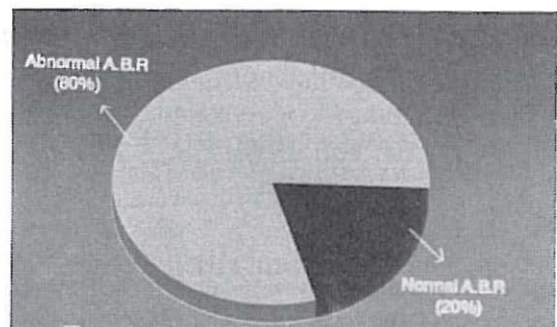


Fig. 4. Normal and abnormal ABR percentages.

neurologic examination, pure-tone and speech audiometry, and bilateral ABR testing.

ABR was performed with a Madsen 2250 in a sound-proof room. Clicks were used as stimuli. They were administered by shielded TDH-39 earphones. The clicks were presented at 85 dBHL and at rates of 10, 30, 50, and 70 stimuli/sec. Surface silver-silver chloride electrodes were used. The electrodes were placed on the vertex and on each mastoid. The potential between the vertex and mastoid ipsilateral to the stimulus was differentially amplified and band-passed at 125 to 2000 Hz with the contralateral mastoid serving as ground. One thousand twenty-four stimuli with condensation phase were presented monaurally and the potentials were averaged during a 10ms period. To ensure reproducibility for each trace the procedure was repeated. The averaged responses were recorded with an X-Y plotter and the responses of two identical stimulation rounds were

superimposed on each graph. Vertex positive deflections were delineated upwards.

The latency period from the onset of the stimulus generating the click to the various positive peaks and the amplitudes of wave I and V were measured from the negative upward peak to the following positive trough on the monitor with a digital cursor. These measures were compared with normative data from 25 adult subjects (50 ears). Test data that exceeded 3 standard deviations from the normative mean for latencies and V/I ratios of less than one were considered abnormal.

## RESULTS

Pure-tone audiometry results for the entire group of 30 patients with definite MS already confirmed by MRI scanning

## DISCUSSION

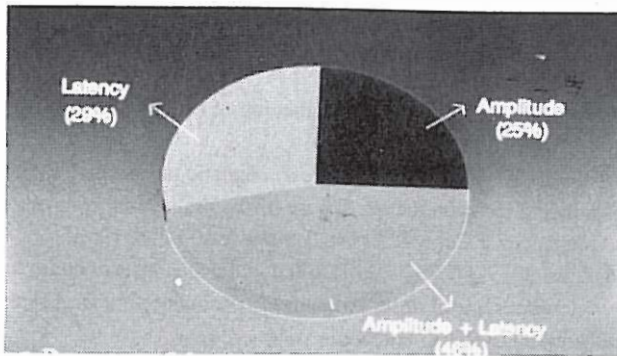


Fig. 5. Percentage of the abnormal latencies to abnormal V/I ratios.

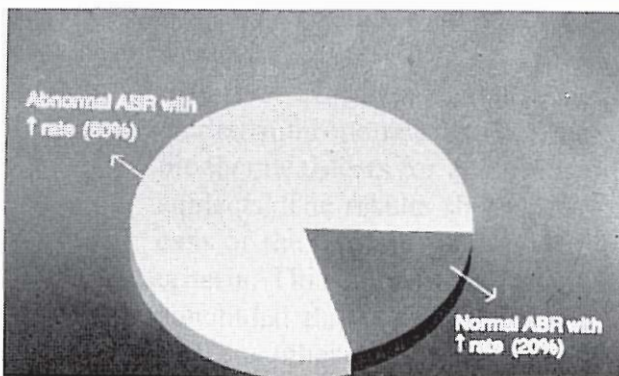


Fig. 6. The effect of an increase in the stimulus repetition rate on ABR.

were as follows: There were 91% sensorineural and 9.0% mixed hearing loss for 10 (33.3%) patients (Fig. 1). The percentage of the type and degree of hearing loss is demonstrated in Fig. 2. Speech audiometry revealed a speech reception threshold greater than 20 dB in 3.0% and less than 20 dB in 97% whilst the speech discrimination score was less than 90% in 3.0% and greater than 90% in 97% of the patients (Fig. 3).

ABRs were performed in all patients and were found to be normal in 6 (20%) and abnormal in 24 (80%) of the patients (Fig. 4). From these 24 patients, 10 patients were affected unilaterally and 14 bilaterally.

From the latency data, it was found that interpeak latency differences I-III and III-V in the low and high brainstem areas were both symmetrically affected; hence I-V intervals were calculated to include both areas. From the amplitude measurements, only waves I and V were found to be affected and their amplitude, ratios were calculated. The percentage contributions of the abnormal latencies to abnormal V/I ratios are shown in Fig. 5.

A significant abnormal response was noted in three patients unilaterally and in 21 bilaterally after increasing the stimulus repetition rate to 30, 50 and 70/sec (Fig. 6).

Patients with definite MS were investigated by MRI and ABR to establish the diagnosis with greater confidence and to exclude other possible causes for symptoms. ABR techniques have an important role in demonstrating clinically silent lesions in the brainstem area,<sup>4,16</sup> and MRI has proved to be of similar value. Recent reports have compared the sensitivity of the two techniques. In one of these,<sup>15</sup> MRI was found superior to other investigative procedures, including ABR, whereas Tramo et al. found ABR studies to be more sensitive than MRI.<sup>11</sup> MRI was also reported to be more sensitive than ABR studies by Runge et al.<sup>10</sup>

We undertook this study to compare the sensitivity of the two techniques in patients in whom the diagnosis was clinically definite. We found that MRI had the same sensitivity as ABR techniques. In 6 of our patients MRI revealed multiple lesions not involving the brainstem. Therefore, ABR studies were normal in this group. Moreover, we anticipate that advances in MRI techniques will increase its sensitivity. Among our 24 (80%) patients with definite MS that involved the brainstem, the two techniques yielded similar results and in the rest of the patients (20%) the lesion was located somewhere else other than the brainstem.

Our data suggest that positive results from the two investigations are often complementary, a substitute for the other. Whether ABR techniques still have a role in the diagnosis of MS when MRI is available is perhaps an economic issue. In 24 of our 30 patients, MRI provided no further information than was obtained by ABR studies, although the cost of MRI is much greater than the cost of ABR. Therefore, it may be appropriate to restrict MRI evaluation to those patients suspected of having MS whose ABR studies are normal.

In this study, ABR abnormalities were common (80%) and showed an excellent correlation with MRI.

Any further studies of MS should first include ABR as it costs less than MRI and is a sensitive predictor of CNS degeneration in MS, but if ABR studies are normal despite a suspicion of having MS, MRI scans should be performed. Moreover, ABRs are routinely used today in the diagnosis of retrocochlear and brainstem lesions. This study also showed that ABR plays an important role in the diagnosis of MS, while the definite diagnosis can be made consequently by the aid of MRI techniques.

## REFERENCES

1. Rose RM, Daly JF: Reversible temporary threshold shift in multiple sclerosis. *Laryngoscope* 74: 424-431, 1964.
2. Brant Zawadzki M, Davis PL: NMR demonstration of cerebral abnormalities: comparison with CT. *AJNR* 4: 117-124, 1983.
3. Lukes SA, Crooks LE: Nuclear magnetic resonance imaging in



## Correlations Between ABR & MRI in MS

- multiple sclerosis. *Ann Neurol* 13: 592-601, 1983.
4. Bartel DR, Marky ON: The diagnosis and classification of multiple sclerosis: Evoked responses and spinal fluid electrophoresis. *Neurology* 33: 611-617, 1983.
5. Sohmer H, Feinmesser M: Cochlear action potentials recorded from the external ear in man. *Ann Otol* 76: 427-436, 1967.
6. Poser CM, Paty DW: New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 13: 227-231, 1983.
7. Robinson K, Rudge P: Abnormalities of the auditory evoked potentials in patients with multiple sclerosis. *Brain* 100: 19-40, 1977.
8. Noffsinger D, Olsen WO: Auditory and vestibular aberrations in multiple sclerosis. *Acta Otolaryngol suppl* 303: 1-36, 1972.
9. Sohmer H, Feinmesser M: Routine use of electrocochleography in human subjects. *Audiology* 12: 167-173, 1973.
10. Runge VM, Price AC: Magnetic resonance imaging of multiple sclerosis. *AJR* 143: 1015-1026, 1984.
11. Tramo MJ, Schneck MJ: Evoked potentials and MRI in the diagnosis of multiple sclerosis. *Neurology* 35 (Suppl 1): 105, 1985.
12. Bydder GM: Clinical NMR imaging of the brain: 140 cases. *AJR* 139: 215-236, 1982.
13. Young IR, Randell CP: Nuclear magnetic resonance (NMR) imaging in white matter disease of the brain using spin-echo sequences. *J Comput Assist Tomogr* 7: 290-294, 1983.
14. Gebarski SS, Gabrielsen TO: The initial diagnosis of multiple sclerosis: clinical impact of magnetic resonance imaging. *Ann Neurol* 17: 469-474, 1985.
15. Crisp DT, Kleiner JE: Clinical correlations with magnetic resonance imaging and multiple sclerosis. *Neurology* 35 (Suppl 1): 137, 1985.
16. Chiappa KH, Harrison JL: Brainstem auditory evoked responses in 200 patients with multiple sclerosis. *Ann Neurol* 7: 135-143, 1980.