Leigh's disease is rather a nosological mess at the present time with cases being reported from various times of life, and with various bits of evidence incriminating different metabolic pathways in the energy generating system. Provided that we keep our eyes firmly fixed on the fact that acute energy deprivation seems to be at its root, and this may come about from various causes, both environmental and genetic, it becomes easier to think constructively about the fundamental nature of the problem.

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References

- Delgado G, Gallego J, Tunon T, Zarrauz JJ, Viñanueva JA. Necrotising haemorrhagic encephalomyelopathy in an adult: ? Leigh's disease. *J Neurol Neurosurg Psychiatry* 1987;50:224-7.
- Riggs HE, Boles RS. Wernicke's disease. A clinical and pathological study of 42 cases. *Q J Alcohol Studies* 1944;30:261-70.
- Jones AR, Ford SA. The action of (s)-alpha-chlorohydrin and 6-chloro-6-deoxyglucose on the metabolism of guinea pig spermatozoa. *Contraception* 1984;30:261-9.
- Herken H, Lange K, Kolbe H, Keller K. Anti-metabolic action on the pentose phosphate pathway in the central nervous system induced by 6-aminonicotinamide. In: Genazzini E, Herken H, eds. *Central Nervous System Studies on Metabolic Regulation and Function*. Berlin: Springer-Verlag, 1974.
- Jacobs JM, Ford WCL. The neurotoxicity and antifertility properties of 6-chloro-6-deoxyglucose in the mouse. *Neurotoxicology (Park Forest II)* 1981;2:405-17.
- Schneider H, Cervos-Navarro J. Acute gliopathy in spinal cord and brain stem induced by 6-aminonicotinamide. *Acta Neuropathol (Berl)* 1974;27:11-232.
- Biaglow JE, Jacobson BE, Nygaard OF. Metabolic reduction of 4-nitroquinoline N-oxide and other radical producing drugs to oxygen reactive intermediates. *Cancer Res* 1977;37:3306-13.
- Rogulja PV, Kovac W, Schmid H. Metronidozol-encephalopathie im der ratte. *Acta Neuropathol (Berl)* 1973;25:36-40.
- Griffin JW, Price DL, Kuethle DO, Goldberg AM. Neurotoxicity of misonidazole in rats. I. Neuropathology. *Neurotoxicology (Park Forest II)* 1980;1:653-66.
- Morgan KT, Gross EA, Lyght O, Bond JA. Morphological and biochemical studies of a nitrobenzene-induced encephalopathy in rats. *Neurotoxicology (Park Forest II)* 1985;6:105-16.
- Philbert MA, Nolan CC, Cremer JE, Tucker D, Brown AW. 1,3-dinitrobenzene-induced encephalopathy in rats. *Neuropathol Appl Neurobiol* 1987; (in press).

The syndrome of irreversible lithium effectuated neurotoxicity

Sir: I read with interest the case report by Tesio *et al*¹ describing a cerebellar syndrome in lithium poisoning. There is a general lack of awareness about irreversible and untreatable complications of lithium treatment² despite evidence to contrary.³⁻⁵ Till recently it has been maintained that the side-effects of lithium are not disabling.² I identified 55 cases of persistent sequelae of lithium therapy after a review of published literature though earlier reviews had given a smaller number.³⁻⁵ Some of the cases of persistent sequelae of lithium therapy have been mistaken for neuroleptic malignant syndrome⁶ owing to a superficial resemblance. Moreover, some cases of longstanding sequelae of lithium therapy may occur without having acute poisoning, a fact which has not been appreciated in earlier reviews.^{3,4} Though most common sequelae are persistent cerebellar symptoms, other clinical manifestations have also been documented. In a typical presentation, acute lithium poisoning precedes the sequelae and the acute phase is generally without cerebellar symptoms.⁴ As consciousness returns the neurological sequelae become more apparent.⁴ In four cases cerebellar signs were present from the beginning of the acute phase in the cases I reviewed. Atypical presentations may include persistent papilloedema, optic neuritis, isolated downbeat nystagmus, peripheral neuropathy and myopathy. Those with atypical presentations are unlikely to have undergone an acute organic brain syndrome. In such cases symptoms develop insidiously while on long-term lithium therapy and persist after discontinuation for varying periods. Prognosis generally is good and in some cases of chronic lithium neurotoxicity the neurological signs may resolve in less than two months after discontinuation.⁷⁻¹⁰ These cases⁷⁻⁹ cannot be termed longstanding according to criteria laid down by Schou.⁴ In general spontaneous recovery may occur in varying degrees over a period of time. Some cases, however, may be unchanged and irreversible. Complete neurological recovery is uncommon but patients may respond to rehabilitative measures with significant functional gains and may return to previous living arrangement.¹¹

I suggest that these persistent sequelae of lithium be called the syndrome of "Irreversible Lithium Effectuated Neuro Toxicity." Extensive demyelination has been found by biopsy of peripheral nerves so involved. It is likely that toxic demyelination at various sites in the central nervous system

especially in the cerebellum may be the mechanism involved in the aetiology of this syndrome.

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References

- Tesio M, Porta GL, Messa E. Cerebellar syndrome in lithium poisoning: a case of partial recovery. *J Neurol Neurosurg Psychiatry* 1987;50:235.
- Editorial. Doubts about the value of lithium maintenance. *Lancet* 1987;i:424.
- Donaldson IM, Cuningham J. Persisting neurologic sequelae of lithium carbonate therapy. *Arch Neurol* 1983;40:747-51.
- Schou M. Long-lasting neurological sequelae after lithium intoxication. *Acta Psychiatr Scand* 1984;70:594-602.
- Adityanjee. Lithium maintenance. *Lancet* 1987;i:866-7.
- Adityanjee. Neuroleptic malignant syndrome or lithium neurotoxicity. *Br J Psychiatry* 1987;150:568-9.
- Lewis DA. Unrecognised chronic lithium neurotoxic reactions. *JAMA* 1983;250:2029-30.
- Slonim R, McLarty B. Six cranial nerve palsies: unusual presenting symptom of lithium toxicity. *Can J Psychiatry* 1985;30:443-4.
- Saul RF, Hamburger HA, Schorst JB. Pseudotumour cerebri secondary to lithium carbonate. *JAMA* 1985;253:2869-70.
- Pesando P, Nuzzi G, Maraini G. Bilateral papilloedema in long-term therapy with lithium carbonate. *Pharmako Psychiatr Neuro psychopharmacol* 1980;13:235-9.
- Izzo KL, Brody R. Rehabilitation in lithium toxicity: case report. *Arch Phys Med Rehabil* 1985;66:779-82.

Tesio replies:

I agree with Dr Adityanjee's suggestion that we recognise the persistent sequelae of lithium poisoning as a syndrome to be named the syndrome of irreversible lithium effectuated neurotoxicity.

First, however, I think we should state more definitely the specific features of this syndrome and the minimal criteria for its diagnosis.

The case I and my coworkers described in a previous paper,¹ the review of the Literature²⁻⁴ and Dr Adityanjee's letter itself suggest that only persistent neurological deficits following acute intoxication could form specific syndrome pathognomonic for lithium poisoning. Minimal