will follow a set of binomial distributions and these will have different standard deviations, another departure from the usual simple regression model. The logit and probit transformations do not help with this and they call for a rather complicated form of weighted

regression (this also has to cope with observed proportions of 0 or 100% for which the transformed values are infinite). There are good computer programs available for implementing this, notably the GLIM and GENSTAT packages.

Startle disease

I think of it as the stiff baby syndrome but it seems that the in-crowd are now calling it familial startle disease or hyperreflexia. A faint echo from a previous incarnation reminds me of the 'jumping Frenchmen of Maine'. It is an autosomal dominant condition presenting usually in the newborn with either muscle rigidity or episodes of stiffening and apnoea often misdiagnosed as epileptic seizures. An exaggerated response to glabellar tap is characteristic and the jerks and spasms are inhibited by tight swaddling or trunk flexion.

Two recent publications throw further light on the syndrome. A paper from America (Stephen G Ryan and colleagues, *Annals of Neurology* 1992; 31: 663-8) describes 30 affected people in five generations of a single family. All were hypertonic at birth and feeding difficulty was common as were inguinal and umbilical hernias, presumably caused by raised intra-abdominal pressure. Four babies died from apnoea due to intense muscular spasm. Motor development was delayed in the early years but improved later as the stiffness regressed and most of the affected individuals were of normal intelligence. In adults the major complaint is of sudden falls caused by transient intense muscle spasm with inability to extend the arms, resulting in frequent head and face injuries. (Look for the scars on the parents' faces.) In this American series 16 patients were treated with clonazepam, all apparently with 'dramatic' improvement. Genetic linkage studies on this family put the gene on the long arm of chromosome 5 linked to a marker locus (colony stimulating factor receptor or CSFIR) at 5q 33-q 35. Several genes are known to be located in this region including one which encodes a subunit of the gamma-aminobutyric acid (GABA) receptor.

From the Hammersmith Hospital in London Dr Lilly Dubowitz and her colleagues (*Lancet* 1992; 340: 80-1) describe a baby with this condition who was at first thought to be suffering from neonatal epilepsy. They measured the concentration of free GABA in the cerebrospinal fluid at 14 days and found it to be low compared with previously published data. The baby improved on treatment with clonazepam and at nine weeks the GABA in the cerebrospinal fluid was within the normal range.

The basic disorder in startle disease is not understood and the neuropharmacology and neurochemistry are complex. Clonazepam is a serotonin antagonist and an excess of serotonergic transmission in the medullary and pontine reticular formation could, apparently, explain the condition. GABA, of course, is an important inhibitory neurotransmitter and the finding of low cerebrospinal fluid GABA is an interesting clue. Dubowitz and colleagues suggest that clonazepam might work by increasing the sensitivity of the GABA receptor though they don't explain how it might do that.

Clearly the hunt is well and truly on for the explanation of this rare but fascinating disease.

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