BENIGN MYALGIC ENCEPHALOMYELITIS

Dear Sir,

An epidemic of benign myalgic encephalomyelitis occurred in the north of England a few months before the Royal Free Hospital was involved. The basic clinical picture of lymphadenopathy, pyrexia, liver and splenic tenderness, with objective neurological changes in 20 per cent of the cases, was similar in both parts of the country. The most likely explanation appeared to be a country-wide infectious illness until Drs. McEvedy and Beard suggested that the Royal Free epidemic was due to hysteria (British Medical Journal, 1970, i, 7) and reaffirmed their idea in their recent report in your Journal (122, February, p. 141). On reading Dr. A. L. Wallis’s account (M.D. Thesis, University of Edinburgh, 1967) of the effect of the epidemic on his practice at Dalston, Cumberland, for evidence of mass hysteria, one finds that he describes an illness resembling glandular fever, with morphological changes in lymphocytes in 30 per cent cases but with negative Paul Bunnell tests. The epidemic started amongst primary school children, with maximal incidence in boys age 5 to 11, but by March and April 1955, had spread to adults, who in general were more severely affected. Some patients showed evidence of either upper or lower motor neurone lesions, with patches of tenderness in the muscles of the legs and hyperaesthesiae in the overlying skin. Mental depression was common, with sleep inversion in some cases. The hysterical features emphasized in the Royal Free cases by Drs. McEvedy and Beard appeared to be infrequent, though temper tantrums in young children were common. Comparison of the two epidemics suggests that the infectious illness in the north did spread south to affect the Royal Free Hospital, but in the circumscribed population of young female adults hysterical reactions were more frequent, especially amongst nurses with a past history of mental illness.

Dr. S. B. G. Innes has suggested (Lancet, 1970, i, 969) that the involvement of the central nervous system in this condition is allergic in nature. This could explain why an agent could be transferred to rhesus monkeys from patients involved in the Adelaide epidemic (Pellew, R. A. A., and Miles, J. A. B. (1955), Medical Journal of Australia, 48, ii, 480) but could not be retransmitted. The recurrences may be the result of a self-perpetuating immunological mechanism precipitated by the infection in susceptible individuals, as may be the case in rheumatoid arthritis. Certainly, in Drs. McEvedy and Beard’s follow-up of cases there is evidence of hypersensitivity reactions such as asthma, eczema and possibly thrombocytopenic purpura in probands and their families.

Acceptance of the hysteria hypothesis presents two dangers. First, the search for an underlying aetiological agent may be abandoned. Some of the cases of the benign myalgic encephalitis syndrome in Japan were found to be due to sensitivity to the drug clioquinol. Secondly, the patient may be labelled a hysteric and denied the assistance he would get if it was considered he had an organic disability. The few patients with this syndrome referred to this centre in recent years have responded to a programme of graded physical activity in a similar manner to those with other organic diseases of the central nervous system.

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MYASTHENIA GRAVIS AND SCHIZOPHRENIA—A RARE COMBINATION

Dear Sir,

We were very interested in the paper in the March 1973 (pp. 343-4) issue by Drs. Gittleson and Richardson on a case of schizophrenia and myasthenia gravis, because we have ourselves recently had such a case.

A married woman of 51, was first seen in her home in the evening of 18 October 1972. She was shaking with terror and unable to face another night in her house because of the things she felt the neighbours were doing to her with electrical machines through the walls and so on. She was forthwith admitted to...
hospital. There was a history of increasing un
ease, with onset of delusions and hallucinations
of a paranoid nature, especially during the previous
seven days.

A diagnosis of myasthenia gravis had been made
in June 1971, and the patient had been established
on a regime including 'Mestinon', prostigmin and
atropine. For a few weeks after she was seen the
myasthenia appeared to become uncontrolled and
the dosage of anti-myasthenic drugs had been
increased.

When admitted she was hallucinated, deluded,
depressed and very anxious. The degree of fear she
showed seemed so unusual that we wondered for a
considerable time whether her condition could be a
toxic state caused by the anti-myasthenic drugs, but
there was no element of confusion. Within three
days the psychotic symptoms and signs disappeared; her
myasthenia, which had at times seemed quite severe,
came under control, and she was discharged home on
13 November 1972, after trial weekend leave. She
had apparently recovered from the psychotic episode,
and the myasthenia was under control with almost
exactly the same dosage of anti-myasthenic drugs as
before the acute psychosis. She had had no anti-
psychotic treatment other than her admission to the
hospital and general nursing care.

Within three days of discharge she relapsed and
had to be re-admitted. She had once again become
hallucinated, deluded and terrified. The myasthenia
was again out of control. This time she was treated
with phenothiazines and later with antidepressives.
The anti-myasthenic drugs were continued. The
symptoms of both disorders again abated very
rapidly, and after a more prolonged period of
observation and trial leave, she was discharged on
18 January 1973, and has done well since.

We are now left wondering whether it was the
schizophrenic illness that caused the myasthenia to
go out of control, because the latter fluctuated pari
passu with the former. (Unit No. 13956/72.)

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AN EXPLANATORY STATISTICAL MODEL
FOR PLASMA LEVELS OF IMIPRAMINE
AND DESMETHYLIMIPRAMINE DURING
LONG-TERM THERAPY

DEAR SIR,

In 1967, in this Journal, Moody, Tait, and
Todrick (1) presented plasma levels of imipramine
and desmethylinipramine (DMI) in 24 patients
receiving long-term imipramine therapy. Because of
'considerable variations in the plasma imipramine
and DMI levels', they concluded that these levels
'were not primarily related to the dosages of
imipramine given'. We have considered Moody's
conclusion of a lack of dose response and have
addressed ourselves to the problem of identifying
what factors relate to the plasma levels.

In addition to plasma levels, Moody presented
sex, age, weight, dose, time after commencement of
therapy, and other drugs the patients were taking.
To enable us to compare dosages for persons of
different body weights, we expressed dosages as

\[ Y = Q(aS + bA + cT) \]

where \( a, b, \) and \( c \) are constants to be determined

- \( S \) is the patient's sex: +1 for males, −1 for
  females
- \( A \) is the patient's age (years)
- \( T \) is the patient's time after commencement
  of therapy (months)
- \( Y \) is the patient's plasma level of imipramine,
  DMI, or total (mcg./l).

The concurrent medication was not considered
because of its variety, and a lack of knowledge of
how it can be incorporated into the mathematical
model.

The regression analysis yielded estimates for
coefficients and their probabilities as below:

The multiple correlation coefficient \( R \), which is the
fraction of the total variation explained by the model,
was computed. For imipramine, DMI, and total, the
observed \( R^2 \) (unadjusted for the mean) were 0.83,
0.92, 0.93 respectively, and all are significant at the
1 per cent level.

<table>
<thead>
<tr>
<th>Category</th>
<th>Imipramine</th>
<th>DMI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Sex</td>
<td>−2.94 (P = 0.860)</td>
<td>−67.34 (P = 0.019)</td>
<td>−70.28 (P = 0.045)</td>
</tr>
<tr>
<td>(b) Age</td>
<td>1.57 (P &lt; 0.001)</td>
<td>3.55 (P &lt; 0.001)</td>
<td>5.18 (P &lt; 0.001)</td>
</tr>
<tr>
<td>(c) Time</td>
<td>2.35 (P = 0.249)</td>
<td>9.91 (P = 0.005)</td>
<td>12.26 (P = 0.006)</td>
</tr>
</tbody>
</table>