Serum fatty acids in multiple sclerosis

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Although much work has been done on the levels of cholesterol, cholesterol esters, and the various phospholipids in the blood and in the brain of patients with multiple sclerosis, little attention has so far been paid to the nature and proportions of the different fatty acids present as cholesterol esters or as components of the different phospholipids.

In 1963, however, Baker, Thompson, and Zilkha reported briefly on the fatty acid composition of lecithin fractions extracted from the white matter of six normal brains and of nine brains from patients with multiple sclerosis. The areas of white matter dissected from the brains of patients with multiple sclerosis appeared normal on inspection, and in no case was tissue taken from the immediate vicinity of a recognizable plaque. The findings appeared to indicate a shift towards greater saturation of the fatty acids in this fraction of the white matter in multiple sclerosis, the percentage of palmitic acid being increased and those of palmitoleic and arachidonic acids decreased.

Since the publication of these results Gerstl, Tavaststjerna, Hayman, Smith, and Eng (1963) have also described a study of the fatty acids in human brains, in which they found that the levels (expressed as m-moles/100 g. wet weight of brain) of both saturated and unsaturated fatty acids in the unfractionated lipids of white matter from one multiple sclerosis brain were slightly lower than the mean levels obtained from three normal brains.

In discussing their own findings Baker et al. (1963) suggested that the changed proportions of fatty acids in brain lecithins in multiple sclerosis could be due to some purely local cause, such as an abnormality of lecithin synthesis or degradation, or could arise as a result of some more general cause, such as a change in the relative amounts of saturated and unsaturated fatty acids reaching the brain. We are therefore now reporting the results of a study of the percentage fatty acid composition of the total lipid extract of serum taken from patients with multiple sclerosis and from control subjects.

**EXPERIMENTAL**

**SUBJECTS** The subjects of the present study comprised 38 controls and 47 patients with multiple sclerosis.

**TABLE I**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr.)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.C.</td>
<td>25</td>
<td>Idiopathic epilepsy</td>
</tr>
<tr>
<td>J.B.</td>
<td>21</td>
<td>Myasthenia gravis</td>
</tr>
<tr>
<td>H.D.</td>
<td>49</td>
<td>Subarachnoid haemorrhage from leaking aneurysm three weeks previously</td>
</tr>
<tr>
<td>N.S.</td>
<td>40</td>
<td>Wilson's disease</td>
</tr>
<tr>
<td>M.A.</td>
<td>47</td>
<td>Essential hypertension</td>
</tr>
<tr>
<td>H.W.</td>
<td>54</td>
<td>Generalized cerebrovascular disease</td>
</tr>
<tr>
<td>L.C.</td>
<td>50</td>
<td>Paralysis agitans</td>
</tr>
<tr>
<td>B.D.</td>
<td>63</td>
<td>Glomus jugulare tumour with hypertension</td>
</tr>
<tr>
<td>B.H.</td>
<td>37</td>
<td>Motor neurone disease</td>
</tr>
<tr>
<td>M.E.</td>
<td>68</td>
<td>Traumatic cervical cord lesion with paraplegia, two weeks previously</td>
</tr>
<tr>
<td>A.P.</td>
<td>27</td>
<td>Dejerine-Sottas' hypertrophic polyneuropathy</td>
</tr>
<tr>
<td>B.L.</td>
<td>32</td>
<td>Dermatomyositis</td>
</tr>
<tr>
<td>F.J.</td>
<td>25</td>
<td>Myasthenia gravis</td>
</tr>
<tr>
<td>D.K.</td>
<td>56</td>
<td>'Drop attacks'</td>
</tr>
<tr>
<td>C.C.</td>
<td>13</td>
<td>Subacute sclerosing leucoencephalitis</td>
</tr>
<tr>
<td>P.F.</td>
<td>45</td>
<td>Motor neurone disease</td>
</tr>
<tr>
<td>W.C.</td>
<td>52</td>
<td>Motor neurone disease</td>
</tr>
<tr>
<td>G.P.</td>
<td>39</td>
<td>Prolapsed intervertebral lumbar disc four weeks previously</td>
</tr>
</tbody>
</table>

The controls included 20 healthy subjects (10 males and 10 females) aged 20 to 52 years (mean, 35 years), and 18 'neurological controls' (five males and 13 females), i.e., in-patients at the National Hospital, Queen Square, the Cheshire Foundation Home for the Chronic Sick (Copthorne, Sussex), and Guy's Hospital, suffering from neurological disorders (Table I) other than multiple sclerosis, and whose ages ranged from 13 to 68 years (mean, 41 years).

The 47 patients with multiple sclerosis, aged 17 to 59 years (mean, 37 years), comprised 38 in-patients (13 males and 25 females) from the same institutions as the controls, and nine out-patients (six males and three females) attending the National Hospital.

Blood (20 ml.) was drawn from each subject from the antecubital vein after an overnight fast; in the case of the female subjects it was drawn between approximately the 12th and the 20th days of the menstrual cycle. For the most part the specimens were drawn in pairs, one from a control and one from a patient with multiple sclerosis, and the subsequent manipulations and analyses carried through 'blind' on each pair. The 'neurological controls' were chosen, as far as was possible, so as to be of the same sex and of a similar age and weight, and showing a degree of physical handicap comparable to that of the multiple sclerosis patients. Any patients, either with multiple sclerosis or other neurological disorder, who
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were unable to take a normal diet were excluded from this study.

**ANALYTICAL METHODS**  After drawing the specimens the blood was kept at room temperature for five hours. The serum was then separated and a total lipid extract prepared according to the procedure of Sperry and Brand (1955).

A sample of each total lipid extract (= 1 ml. serum) was evaporated to dryness and the residue hydrolysed in 2 ml. N KOH in 90% ethanol for 30 min. at 37°. The hydrolysate was then diluted with 5 ml. water, acidified with 1-5 ml. 2N HCl and the fatty acids extracted into 10 ml. diethyl ether.

The ether extract of the fatty acids was then evaporated to dryness, and the fatty acids methylated by reaction with 1 ml. 2% (w/v) H2SO4 in methanol at 60°C. for at least 10 min., after which the mixture was diluted with 4 ml. water and the methyl esters extracted with 5 ml. ether. The final ether extract was dried with anhydrous Na2SO4 for gas chromatography using a Perkin-Elmer model 800 instrument fitted with a 6 ft. copper column (1 mm. bore) packed with 80-100 mesh acid-washed celite coated with 20% (w/w) of the polyester diglycoladipate resin LAC-IR-296. Separations were carried out at 190°. The chromatograms were analysed by triangulation and the proportions of the individual fatty acids expressed as percentages of the total.

**RESULTS**

In the initial stages of this study a comparison was made between the percentage fatty acid composition of the serum lipids from a series of patients with multiple sclerosis, all of whom were in-patients at the National Hospital, and that of a series of healthy control subjects, mostly members of the laboratory staff. Because of the differences of diet and daily activities between these two groups of subjects it was decided in the subsequent work to substitute a group of 'neurological controls' for the healthy subjects; these neurological controls were also all in-patients at the National Hospital, living under the same dietary régime but suffering from a wide range of other neurological disorders. As stated above these controls were chosen, as far as was possible, to match the multiple sclerosis patients as regards overall physical handicap. In the later stages of the work a number of patients with multiple sclerosis attending the National Hospital as out-patients and also a small number of in-patients from one of the Cheshire Homes and from Guy's Hospital were included.

Table II shows the mean values (and the standard errors of the means) for the percentages of the different fatty acids in the mixture of fatty acids obtained from the total lipid extracts of sera from the different groups of subjects. Statistical examination of the values obtained from the healthy subjects and the neurological controls showed that there was no significant difference between these two groups, which have therefore been combined to give one control group of 38 subjects. (Throughout this work we have regarded differences as significant only when P<0.01.) It will be seen that of the different fatty acids measured linoleic acid (18:2) shows the greatest variation in its percentage level in the different groups, the 47 patients with multiple sclerosis showing a mean value of 22.3 as compared with 25.6 for the 38 controls, the difference between these two means being highly significant (P<0.0001). When the multiple sclerosis patients are subdivided into in-patients and out-patients, it will be seen that the 38 in-patients show an even lower mean percentage

<table>
<thead>
<tr>
<th>Group</th>
<th>No. in Group</th>
<th>Fatty Acids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>14:0</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>20</td>
<td>Mean</td>
</tr>
<tr>
<td>Neurological controls</td>
<td>18</td>
<td>Mean</td>
</tr>
<tr>
<td>All controls</td>
<td>38</td>
<td>Mean</td>
</tr>
<tr>
<td>Multiple sclerosis in-patients</td>
<td>38</td>
<td>Mean</td>
</tr>
<tr>
<td>Multiple sclerosis out-patients</td>
<td>9</td>
<td>Mean</td>
</tr>
<tr>
<td>All multiple sclerosis patients</td>
<td>47</td>
<td>Mean</td>
</tr>
</tbody>
</table>

**SIGNIFICANCE OF DIFFERENCES BETWEEN MEANS FOR PERCENTAGES OF LINOLEIC ACID (18:2)**

All controls (38) v. all multiple sclerosis patients (47) : P<0.0001
All controls (38) v. multiple sclerosis in-patients (38) : P<0.0001
All controls (38) v. multiple sclerosis out-patients (9) : no difference
Neurological controls (18) v. all multiple sclerosis patients (47) : P<0.05, >0.02 (not significant)
Neurological controls (18) v. multiple sclerosis in-patients (38) : P=0.004
of linoleic acid (21-5), whereas the nine out-patients have a mean value (25-7) indistinguishable from that of the controls.

The mean percentage of linoleic acid in the 38 multiple sclerosis in-patients is also significantly lower than that of the neurological controls (P = 0.004), although the multiple sclerosis patients as a whole, i.e., in-patients and out-patients, do not show any significant difference in this respect from the neurological controls (P < 0.05, > 0.02).

Because of this difference in the mean values of linoleic acid in the multiple sclerosis in-patient and out-patient groups it was decided next to attempt to grade these patients according to the estimated activity of the disease. The clinical assessment and grading of activity was carried out by one of us (K.J.Z.) without access at the time to the analytical results; in the later stages of the work grading was made before the blood sample was drawn. In a condition such as multiple sclerosis, with its tendency for apparently random and often sudden exacerbations and remissions, assessment of the activity of the disease process at any one time can present extreme difficulty. The chief criterion on which our grading was based was clinical evidence of deterioration in the preceding month, as shown by the development of new signs or symptoms, or by the exacerbation or extension of already existing signs or symptoms. The patients were consequently grouped into the following four grades:

**GRADE I** Patients showing only slight neurological disability, and no evidence of recent deterioration: none were bed-ridden, and seven of the 10 patients falling into this group were seen as out-patients.

**GRADE II** Patients showing evidence of slight recent deterioration: only one (H.S.) of the 11 patients in this group was confined to bed, and two were attending as out-patients.

**GRADE III** Moderate recent deterioration, with evidence of a more severe increase in disability than that shown by the patients in grade II: all were under treatment as in-patients, and only one (F.A.) was confined to bed.

**GRADE IV** Rapid and extensive recent deterioration: all were in-patients and two (J.B. and M.C.) were confined to bed.

Table III lists the percentages of linoleic acid in the serum lipids of each of the 47 patients with multiple sclerosis, subdivided into the four groups of activity. It will be seen that the mean percentage of linoleic acid in the patients falling into grade I of our assessment is indistinguishable from that of the control series, but that it falls progressively with increasing evidence of recent deterioration in the patient's condition.

Since it seemed possible that this decline in the percentage of linoleic acid in the serum lipids might represent merely a non-specific result of increasing disability with a consequent decline in physical activity due to a variety of causes, it was decided to attempt to group the 'neurological controls' into four comparable grades, the chief criterion for the grading of these patients being the degree of disability:

**GRADE I** Only minor degree of physical handicap at the time of, or before the taking of blood: all were ambulant.

**GRADE II** Greater degree of overall physical handicap: two (H.D. and G.P.) of the eight patients in this grade were confined to bed.

**GRADE III** Moderately severe physical handicap, three (N.S., B.H., and A.P.) suffering from progressive neurological disorders, and two of them (B.D. and A.P.) confined to bed.

**GRADE IV** Severely paralysed, two (P.F. and W.C.) with a progressive disorder, and the third (M.E.) confined to bed.
Although the numbers of control patients in the groups are small there does not appear to be any tendency for a decline in the percentage of linoleic acid when this is correlated with overall disability (Table IV).

| TABLE IV |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Grade I          | Grade II         | Grade III        | Grade IV         |
|                  |                  | N.C. 32:1        | F.J. 28:0        | B.H. 27:8        |
|                  |                  | C.C. 25:2        | B.L. 21:0        | B.D. 26:7        |
|                  |                  | H.W. 23:4        | W.C. 22:3        |                  |
| Mean             | 25-5             | 23:0             | 26:0             | 24:4             |

In view of the apparent correlation between activity of the disease in the multiple sclerosis patients and the percentage level of linoleic acid Table V sets out the mean percentage level of the other fatty acids present in the serum lipids of these patients, grouped into the four grades. It will be seen that the percentages of the other fatty acids are on the whole remarkably constant, and show little evidence of any shift in passing from grade I to grade IV. Since these values are all percentages of the total, the lowered percentage of linoleic acid in grade IV is of course reflected in the percentages of the other acids, and it will be noticed that the levels of palmitic acid (16:0), palmitoleic acid (16:1), and oleic acid (18:1) in this grade are each slightly higher than in grade I, palmitic acid in particular being considerably and significantly raised.

**DISCUSSION**

In a study of a condition such as multiple sclerosis, the clinical course of which is so varied and usually characterized by remissions and exacerbations, it is desirable to study a relatively large group of patients.

Because of this, and because in the early stages of the work we wished to avoid if possible the time-consuming column-fractionation of the serum lipids, a start has been made by measuring the percentage composition of the mixture of fatty acids in the hydrolysate of a total lipid extract of fasting serum.

The use of fasting serum has the disadvantage that, as was shown by Dole (1956), the concentration of non-esterified fatty acids in the plasma will be high. Despite this, however, it was decided initially to use subjects in the post-absorptive state, particularly since it was our intention, after having studied the fatty acid composition of the unfractionated serum lipids, to proceed to an examination of the separated cholesterol ester, phospholipid, and triglyceride fractions; the results of our study of these individual fractions will be described elsewhere, but a preliminary statement of our findings so far is included below.

As mentioned earlier, the proportion of linoleic acid in the unfractionated total lipid extract shows the greatest significant variation in the different groups of subjects. As, however, the healthy controls and the neurological controls showed no significant difference in the percentage of this acid they have been listed together as one control group of 38 subjects. The percentages of the different fatty acids found in our control group agree closely with the values given by Tuna, Logothetis, and Kammerack (1963a) for 11 ‘normal’ persons (patients suffering from tension headaches, psychoneurotic states, and benign prostatic hypertrophy) after an overnight fast.

The 38 controls have also been examined to discover whether the sexes show any difference in the percentage of linoleic acid. Taking the group as a whole, the mean percentage (± S.E.M.) for the 15 men (24·5 ± 0·6) is not significantly different from that for the 23 women (26·4 ± 0·7). Neither is there any difference between the mean percentages for males and females in the group of neurological controls. In the case of the 20 healthy subjects,

**TABLE V**

<table>
<thead>
<tr>
<th>Grade</th>
<th>No. of Subjects</th>
<th>14:0</th>
<th>16:0</th>
<th>16:1</th>
<th>18:0</th>
<th>18:1</th>
<th>18:2</th>
<th>20:3</th>
<th>20:4</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>10 Mean</td>
<td>1·1</td>
<td>23·8</td>
<td>3·8</td>
<td>4·7</td>
<td>28·3</td>
<td>25·8</td>
<td>1·7</td>
<td>5·2</td>
<td>5·6</td>
</tr>
<tr>
<td></td>
<td>S.E.M.</td>
<td>0·1</td>
<td>0·5</td>
<td>0·4</td>
<td>0·8</td>
<td>0·8</td>
<td>0·9</td>
<td>0·2</td>
<td>0·2</td>
<td>—</td>
</tr>
<tr>
<td>II</td>
<td>11 Mean</td>
<td>1·3</td>
<td>23·2</td>
<td>4·0</td>
<td>5·6</td>
<td>30·1</td>
<td>23·6</td>
<td>1·6</td>
<td>5·3</td>
<td>5·3</td>
</tr>
<tr>
<td></td>
<td>S.E.M.</td>
<td>0·1</td>
<td>0·3</td>
<td>0·1</td>
<td>0·2</td>
<td>0·2</td>
<td>0·6</td>
<td>0·1</td>
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<tr>
<td>III</td>
<td>16 Mean</td>
<td>1·2</td>
<td>23·9</td>
<td>4·5</td>
<td>4·5</td>
<td>32·1</td>
<td>21·6</td>
<td>1·6</td>
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<tr>
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<td>0·1</td>
<td>0·8</td>
<td>0·2</td>
<td>0·4</td>
<td>0·5</td>
<td>0·6</td>
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<td>—</td>
</tr>
<tr>
<td>IV</td>
<td>10 Mean</td>
<td>1·2</td>
<td>27·6</td>
<td>5·5</td>
<td>4·6</td>
<td>30·2</td>
<td>18·6</td>
<td>2·2</td>
<td>5·4</td>
<td>4·7</td>
</tr>
<tr>
<td></td>
<td>S.E.M.</td>
<td>0·1</td>
<td>0·9</td>
<td>0·7</td>
<td>0·5</td>
<td>1·0</td>
<td>0·4</td>
<td>0·2</td>
<td>0·3</td>
<td>—</td>
</tr>
</tbody>
</table>
however, the mean for the 10 men (25.3 ± 0.8) is significantly lower (P<0.01) than the mean for the 
10 women (28.4 ± 0.6).

Lawrie, McAlpine, Pirrie, and Rifkind (1961), in a 
study of fatty acid patterns in human serum in health, 
found a significantly lower level of linoleic acid in 
the triglyceride fraction from male subjects, but no 
significant differences were found in the composition 
of the cholesterol ester or phospholipid fractions; 
although they also reported significantly lower levels 
of palmitic acid and higher levels of arachidonic acid 
in the triglyceride fraction of male subjects. we have 
not found any differences between the sexes in the 
percentage levels of these two acids in the total 
sodium lipids.

In Table III the 47 patients with multiple sclerosis 
have been separately listed as males and females 
in each of the four grades into which they have been 
grouped; although, when subdivided in this way, 
some of the groups are small, no significant differ-
ence in the percentage level of linoleic acid between 
the sexes emerges in any of the grades.

The group of healthy controls is the only one that 
appears to show a difference in this respect between 
the sexes, the women having a slightly higher per-
centage of linoleic acid in the serum lipids than the 
men. However, as the female patients with multiple 
sclerosis who were showing signs of rapid and 
extensive recent deterioration (grade IV, Table III) 
possess percentage levels of linoleic acid which on 
average are actually lower than the mean percentage 
in the grade IV males, this apparent sex difference in 
the healthy controls certainly does not influence our 
conclusion that in active multiple sclerosis there is 
evidence that the percentage of this fatty acid is 
low.

As shown in Table III, an attempt to group the 
multiple sclerosis patients into grades, based on the 
overall clinical assessment of the activity of the 
disease, shows that, in general, the lowest values for 
the percentage of linoleic acid occur among those 
patients showing evidence of clinical deterioration 
in the preceding month. It is of interest to note that 
one of the grade I patients (M.G.) had an unusually 
low proportion (19.7%) of linoleic acid for this grade 
as a whole; although this patient had been allocated 
to grade I on admission, blood was drawn only after 
she had been in the ward for five days, and during 
the course of the next two weeks it became obvious 
that her clinical condition had deteriorated. Patient 
C.C. was put into grade I of the neurological controls 
(Table IV) since her only symptoms at the time of 
examination were due to epileptiform seizures; over 
the subsequent four weeks her condition worsened 
and the diagnosis of subacute sclerosing leucoen-
cephalitis was established.

We have been able to find only two reports on the 
proportions of fatty acids in the serum lipids of patients with multiple sclerosis. Gerstl, Davis, Smith, 
Ramorino, and Orth (1957) measured serum dienoic 
fatty acids by the method of alkali isomerization in 
11 patients with active multiple sclerosis, nine patients 
with inactive multiple sclerosis, and eight control 
subjects. Although the level (mg./100 ml.) of dienoic 
fatty acids was considerably higher in patients with 
the inactive disease than in those in the active state, 
there was no difference between the values found in 
the latter group and that in the controls. Tuna, 
Logothetis, and Kammerreck (1963b) studied a group 
of seven patients with multiple sclerosis, all of whom 
had at the time an acute exacerbation of their disease, 
and found that the percentage of linoleic acid in the 
serum lipids did not differ significantly from normal. 
Our results are therefore at variance with those of 
these latter workers; it must, however, be pointed 
out that in our group of 47 patients with multiple 
sclerosis there is a wide scatter in the values found 
for the proportion of linoleic acid, varying from 
29.8% down to 16.3%. Moreover the normal values 
obtained in our out-patient group, together with the 
correlation that appears to exist between the pro-
portion of this fatty acid and the activity of the 
disease (Table III), stresses the need for a close 
alignment of biochemical results with the clinical 
assessment of the condition in a disease as variable 
in its course as multiple sclerosis.

Tuna et al. (1963b) also found a statistically sig-
ificant reduction in the percentage of palmitic acid 
in their group of seven patients with multiple sclero-
sis when compared with a series of 11 control sub-
jects reported on earlier (Tuna et al., 1963a). We are 
at a loss to explain the difference between their 
results and our finding of a statistically significant 
rise in the percentage of palmitic acid in our grade IV 
patients as compared with grade I (Table V).

The results described above on unfractionated 
serum lipids have yielded information only about 
the percentage fatty acid composition of these lipids. 
Such information is difficult to interpret unless 
measurements are also made in terms of absolute 
quantities of the acids present. We are now carry-
ning out such a study on the separated cholesterol ester, 
phospholipid, and triglyceride fractions. These 
results will be described later, but already we have 
evidence that in the active phases of multiple 
sclerosis there is a lowering of the level of linoleic 
acid (µEq./ml.serum) in the cholesterol ester fraction, 
in which a large proportion of the plasma linoleic 
acid is known to occur (Lipsky, Haavik, Hopper, 
and McDivitt, 1957; Dole, James, Webb, Rizack, 
and Sturman, 1959; Lawrie et al., 1961).

When we turn to the interpretation of this apparent
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from that of the rest of Great Britain, whereas that of the Faroe Islanders contains whale meat and blubber (containing mostly unsaturated fatty acids), uncooked dried mutton, more fowl (puffins), and much more fish. Although, when contrasted with the prevalence of the disease in other parts of Great Britain, it is clear that other factors must be involved, these epidemiological observations are consistent with the conception that the availability of unsaturated fatty acids may be one factor determining the prevalence in otherwise susceptible persons. Restriction of dietary intake of unsaturated fatty acids, however, is clearly not the only means by which a low level of linoleic acid in the serum might ensue, and it is certainly not suggested that a purely dietary deficiency of unsaturated fatty acids was the precipitating cause of exacerbations in our series of patients.

Alternatively, it is possible that the low proportions of plasma linoleic acid might arise from some local cause in the central nervous system or elsewhere resulting in a change in the rate of uptake of linoleic acid from the plasma or in its rate of entry into the plasma. On present evidence, however, it is not possible to do more than speculate on the nature of the abnormality underlying our findings.

**SUMMARY**

A study has been made of the percentage fatty acid composition of the total lipid extract of serum taken from 47 patients with multiple sclerosis and from 38 control subjects.

It has been found that the percentage of linoleic acid (18:2) shows a statistically significant reduction in the multiple sclerosis group as a whole, the mean value for the controls being 25.6% of the total fatty acids and for the multiple sclerosis patients 22.3%.

When the patients are graded according to the activity of the disease, the percentage of linoleic acid is found to fall progressively with increasing evidence of recent deterioration in the patient’s condition, the mean level in the 10 patients placed in the grade showing the greatest deterioration being 18.6%.

The possible significance of these findings is briefly discussed.

We wish to thank the physicians in charge of the patients for their kind cooperation in this work. Our thanks are also due to the Multiple Sclerosis Society for a grant for the purchase of a Perkin-Elmer gas chromatograph, to the Medical Research Council for technical assistance, to Dr. B. McArdle and Dr. G. R. Webster for many helpful discussions, and to Miss L. Whibley, Miss P.
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