

TABLE I.—*Inhibition of the P.P.D.- and Thyroid-induced Lymphocyte Response by Fatty Acids in Normal Subjects and M.S. Patients, measured with the Macrophage Electrophoretic Mobility Test*

Subject No.	P.P.D.							Thyroid Antigen								
	No Fatty Acids	C 18 : 1			C 18 : 2		C 20 : 4		No Fatty Acids	C 18 : 1			C 18 : 2		C 20 : 4	
		% Slowing* (a)	% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†		% Slowing* (a)	% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†
Normal Subjects																
1	18.3	17.8	2.7	7.1	61.2	—	—	—	—	—	—	—	—	—	—	
2	17.5	16.0	8.6	6.3	64.0	3.4	82.0	—	—	—	—	—	—	—	—	
3	17.6	16.6	5.7	6.6	62.5	3.8	78.4	—	—	—	—	—	—	—	—	
4	18.2	17.5	3.8	7.2	60.4	3.6	80.2	19.6	18.7	4.6	8.5	57.0	4.5	72.0	—	
5	17.4	17.2	1.2	6.6	62.1	3.7	78.8	—	—	—	—	—	—	—	—	
6	17.5	17.0	2.7	6.9	60.5	4.2	76.0	19.5	18.6	4.6	8.8	54.9	4.5	76.9	—	
7	18.1	17.8	1.7	7.2	61.2	3.6	80.1	19.8	19.6	1.0	9.7	50.0	6.6	67.0	—	
8	18.3	18.2	0.5	7.0	61.7	3.8	79.2	—	—	—	—	—	—	—	—	
M.S. Patients																
9	17.7	17.5	1.1	2.9	84.0	0.9	95.0	—	—	—	—	—	—	—	—	
10	14.1	13.8	2.1	1.8	87.2	0.8	94.3	—	—	—	—	—	—	—	—	
11	11.2	11.0	1.8	1.3	88.4	0.3	97.3	—	—	—	—	—	—	—	—	

*Reduction of macrophage mobility brought about by lymphocyte-antigen reaction.

†Percentage change in macrophage slowings calculated: $\frac{a-b}{a} \times 100$.TABLE II.—*Inhibition of the Encephalitogenic-Factor-induced Lymphocyte Response by Fatty Acids in M.S. Patients and Patients with Other Neurological Diseases Measured With the Macrophage Electrophoretic Mobility Test.*

Case No.	No Fatty Acids % Slowing* (a)	C 18 : 1		C 18 : 2		C 20 : 4	
		% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†	% Slowing* (b)	% Inhibition†
Multiple Sclerosis							
9	18.4	17.9	2.7	1.9	87.7	1.2	93.5
10	14.7	14.4	2.0	1.8	87.7	0.6	96.0
11	14.8	14.3	3.4	1.8	87.8	0.8	94.6
Other Neurological Diseases							
12	17.2	16.6	3.5	9.4	45.4	5.4	68.6
13	14.7	14.5	1.4	7.7	47.6	4.5	69.4
14	18.3	17.9	2.2	9.8	46.4	5.6	69.4

*Reduction of macrophage mobility brought about by lymphocyte-antigen reaction.

†Percentage change in macrophage slowings calculated: $\frac{a-b}{a} \times 100$.

improvement in clinical course in a group of patients treated over a two-year period. Several investigations have revealed significant alterations in the fatty acid composition of brain lipids^{1,2} and of the serum^{3,4} M.S., so that the effect of such a diet might be regarded as an attempt at substitution therapy. However, the results of Turnell *et al.*⁵ indicate that free fatty acids may play an important part in the immunosuppressive effect of corticosteroids, and so it seemed possible that the increase of the linoleate serum level might have an immunosuppressive effect in these patients.

To test this hypothesis we studied the effects of oleic acid (C 18:1), linoleic acid (C 18:2), and arachidonic acid (C 20:4) on the human lymphocyte response to three antigens—purified protein derivative of tuberculin (P.P.D.), encephalitogenic factor, and thyroid antigen (F₁ + F₂), using the macrophage electrophoretic mobility test.^{6,7} In this test the percentage slowing of normal guinea-pig macrophages in an electric field measures lymphocyte-antigen interaction. It is these percentages which are shown in tables I and II. Lymphocytes from normal subjects as well as from patients with M.S. and other neurological diseases were studied.

With a dosage of fatty acid of 0.08 mg/ml (corresponding to the normal serum level of unesterified oleic and twice the normal level of unesterified linoleic acid) we found a significant inhibition caused by both linoleic

and arachidonic acid, whereas oleic acid was virtually without effect. The inhibition occurred only when the fatty acids were added to the lymphocytes before the antigen. When antigen was allowed to interact with the lymphocytes for 1.5 min and linoleic acid was then added no inhibition was to be observed, suggesting that the acid may inhibit the recognition of antigen by the lymphocytes. The interference with lymphocyte-antigen interaction by linoleic and arachidonic acid occurred not only with P.P.D. and thyroid as antigens in normal subjects (table I) but equally with P.P.D. and encephalitogenic factor in M.S. patients and those with other neurological diseases (tables I and II). The percentage inhibition was higher in M.S. patients than in the control groups.

In the context of M.S. the present results may offer an explanation for the findings by Dr. Millar and his colleagues of the beneficial effect of linoleic acid treatment. Such treatment might be expected to reduce lymphocyte attack upon brain antigen *in situ* and (if such an autoaggressive process is indeed at the root of M.S. pathogenesis) so hold up the progress of the disease.

Further studies of the possible immunoregulatory effect of unsaturated fatty acids (dependent perhaps on chain length and degree of unsaturation) in normal subjects, in M.S., and in the wider field of clinical immunology are indicated.

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—We are, etc.,

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Fibrinolysis in Cholestatic Jaundice

SIR,—The paper by Dr. A. Jedrychowski and his colleagues (17 March, p. 640) reporting decreased fibrinolytic activity in patients with cholestatic jaundice prompts us to report the preliminary results of a similar study.

Test	Patients Mean \pm S.D.	Normal Values Mean \pm S.D.
Euglobulin lysis time (units/ml)	2.7 \pm 1.1*	12.0 \pm 5.3
Plasminogen (units/100 ml)	99 \pm 22	100 \pm 21
Fibrinogen (mg/100 ml)	636 \pm 192*	350 \pm 84
Factor VIII (%)	218 \pm 66*	104 \pm 23
Antithrombin III (%)	108 \pm 26	100 \pm 10
Thrombin time (sec)	18.0 \pm 3.2†	15.0 \pm 0.4
Reptilase time (sec)	18.1 \pm 1.8†	15.8 \pm 0.9
Normotest (%)	90 \pm 18	94 \pm 16
Thrombotest (%)	39 \pm 27*	90 \pm 15

* $P < 0.001$ † $P < 0.02$

Our findings in 11 patients with large bile duct obstruction of varying aetiology pre-treated with vitamin K before testing are shown in the table. There was a pronounced decrease of plasminogen activator without variations in the plasminogen concentration. Fibrinogen and factor VIII levels were very high; progressive antithrombin (antithrombin III) assayed immunochemically was normal; and the thrombin and Reptilase times, which relate to the last phase of blood coagulation, were significantly prolonged. Normotest and Thrombotest are standardized coagulation tests sensitive to variations in the plasma levels of factors II, VII, and X. In our patients the Thrombotest, which is known to be influenced by coagulation inhibitors, was low, whereas the Normotest, which is affected only by the clotting factor concentrations, gave normal results in the same plasma samples.

The findings of an abnormal Thrombotest and thrombin and Reptilase times suggest the presence in these patients of some degree of inhibition of the clotting mechanisms independent of vitamin K deficiency. We are now trying to discover whether the inhibitory activity may be related to the high levels of bilirubin glucuronides, as suggested by the experimental findings of Kopec *et al.*¹ Therefore, while confirming the finding by Dr. Jedrychowski and his colleagues and other authors^{2,4} of decreased fibrinolysis and high levels of clotting factors in these patients, our results show that other coagulation abnormalities are present in addition to the well-known vitamin K-dependent deficiency of clotting factors.

Dr. Jedrychowski and his colleagues suggest that decreased fibrinolysis may render these patients particularly liable to postoperative venous thrombosis. This view is not supported by the available evidence, which shows that the incidence of deep vein thrombosis after biliary surgery is no higher than after surgical operations of comparable severity.^{5,7} In our experience, bleeding is a greater problem than thromboembolism in these patients.—We are, etc.,

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Simple Finger Tourniquet

SIR,—While working recently as a casualty registrar I had to perform many minor operations on fingers and toes, many of them under ring anaesthesia and some under general anaesthesia. I found that rubber tube finger tourniquets nearly always snapped when the tension was increased beyond the point of obstruction of venous flow, or caused more bleeding if they stayed intact.

A simple alternative method of exsanguinating the digit and applying a good working tourniquet which I devised is to cut off the finger of a disposable glove, cut off its tip as well, stretch and apply it to the finger or toe to be operated on, and roll it proximally to form a ring at the base of the digit. This provides a satisfactory bloodless field for any operation and the ring can be readily cut for removal after surgery.—I am, etc.,

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Australia Antigen in V.D. Clinic Patients

SIR,—Dr. D. J. Jeffries and others (26 May, p. 455) claim to show a difference between the numbers of Australia-antigen-positive patients among those attending a venereal disease clinic and the numbers of Australia-antigen-positive individuals among blood donors.

Blood donors are not a useful group for comparison in this case as they are not representative of the general population. At each attendance potential donors, before being accepted, are asked both if they have ever had jaundice and if they have recently been in contact with a case of jaundice. No such screening method is applied to potential patients at venereal disease clinics.

This observation in no way affects the differences that were found between groups of patients attending the clinic.—I am, etc.,

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Is Your Pain Really Necessary?

SIR,—I was interested in your comments (leading article, 12 May, p. 323) on the aetiology of infantile colic. This common disorder causes much distress to both mother and infant and many visits to the family doctor, who may well be rather baffled by it. Certainly I agree that the theory of the colic being a result of maternal anxiety rather parallels the chicken-egg controversy. What mother would not be anxious when her infant continuously screams, sleeps for only brief periods, and feeds poorly? The

occurrence of these symptoms, together with the predisposition to vomiting and/or diarrhoea, which may be difficult to treat, is sometimes due to cow's milk intolerance. With a history of this disorder and its very difficult weaning period when the infant is first exposed to cow's milk products, the possibility of the two occurrences being related should be borne in mind. The additional presence of flexural eczema would be a certain indication to withdraw cow's milk products for a trial period of three to four weeks and replace them with a synthetic milk substitute such as Nutramigen.

I would add that the term "milk intolerance" is used deliberately and the term "allergy" avoided since there is seldom a true atopic status, and specific circulating or cell-fixed antibodies are not demonstrable; indeed the lesion may be at the level of the intestinal villus, as in lactase deficiency. Many patients with milk intolerance will grow out of their trouble and be able to tolerate milk products in later childhood, often by the fifth or sixth year.

I have often observed children of school age who are of rather small stature, often with obstinate eczema, and frequently with a history of unexplained and various gastrointestinal difficulties extending back to their first year of life, when they were described as "colicky." These children have responded to withdrawal of ingested cow's milk by the losing of their eczema, stopping their gastrointestinal symptoms, and gaining weight and height with gratifying speed. Serum IgE and IgA levels are usually normal, and the skin tests to milk negative. The substitute of cow's milk by goat's milk is quite useless in this condition and the only correct course is to stop milk and milk derivatives completely.—I am, etc.,

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Cardiological Changes and Car Driving

SIR,—The results reported by Dr. W. A. Littler and others (5 May, p. 273) are interesting but one wonders how valid they are.

A clinical assumption (and indeed a lay one) is that prolonged driving in heavy traffic or on motorways can provide a cardiac stress. Very many salesmen and managers drive long distances several times a week to attend to often stressful business affairs, after which they drive home or to another business meeting. To drive for up to 60 minutes two or three times a day is quite a different matter from driving for three hours, working for seven and driving again for another three. Fatigue in itself is a stress, and this plus the effect of either a pounding motorway journey or a trans-London or trans-West Midlands drive would, I believe, if measured, provide quite different figures from those obtained by Dr. Littler and his colleagues. One excludes professional truck drivers since they are self-selected and do not fall into the same category as those who perforce have to drive long distances on top of their normal work; 30,000 miles a year is not uncommon for young managers.

In cases of ischaemic heart disease in younger patients I am now in the habit of taking a driving history, and my impression