I would like to make it quite clear that this is not an attack on my medical colleagues alone. I am aware that many of my pharmacist colleagues are in the same bewildered state as the more unobservant doctor. This is deplorable. I would say that pharmacists who do not know their drugs really ought to ask themselves whether they can, in all conscience, still call themselves "pharmaceutical chemists." I would appeal to all, doctor and pharmacist alike, to take drugs more seriously. If we do not know our tools how can we pick the best for the task in hand and gauge the vigour with which to use them? There are, these days, aids galore—our patients are entitled to expect us to use them.—I am, etc.,

A. P. LAUNCHBURY,
Group Chief Pharmacist,
South Birmingham Hospital Management Committee.
Selly Oak Hospital,
Birmingham.

Diagnosis of Suspected or Occult Pulmonary Embolus

SIR,—Previous histopathological studies have indicated that massive pulmonary embolism may be followed by an episode of fatal disseminated intravascular coagulation.[1] An important question arising from this work is whether low-grade disseminated intravascular coagulation is a common but unrecognized sequela of non-fatal pulmonary embolism. Confirmation of this could be of some importance, as recent technical developments in the diagnosis of occult intravascular coagulation and fibrinolysis, using the tanned red cell haemagglutination immunoassay for the quantitation of serum fibrin/fibrinogen degradation products (F.D.P.), might be used as either supportive evidence of a clinical diagnosis or to detect occult pulmonary embolism. During a pilot study of the changes of serum F.D.P. in response to surgery and acute myocardial infarction evidence was obtained which indicates that such a hypothesis is worthy of further investigation.

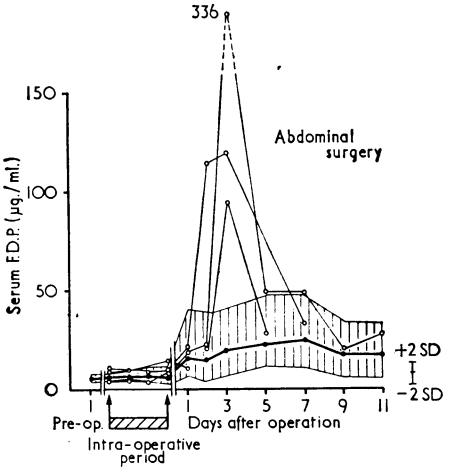

FIG. 1.—The changes of serum F.D.P. in response to abdominal surgery in 11 female patients. The closed circles represent the mean values of eight of the patients and the shaded area the range. The open circles are the values obtained from the remaining three patients (see text). The mean ±2 S.D. values were obtained from 50 healthy age and sex matched resting controls.

The operative group of patients consisted of 11 premenopausal women who, apart from their primary gynaecological complaints, were considered to be healthy. Five underwent total hysterectomy, three partial hysterectomy, and three unilateral salpingo-ophorectomy. Twelve patients were also studied with the clinical diagnosis of acute myocardial infarction, which was subsequently confirmed by electrocardiographic and serum enzyme abnormalities. The first venous blood sample was obtained within six hours of the onset of chest pain. All received oral anticoagulants on admission; none received digoxin or diuretics during the study. The serum F.D.P. immunoassay was performed as described previously.[2,3] The person responsible for the assays had no prior knowledge of the source of the serum samples.

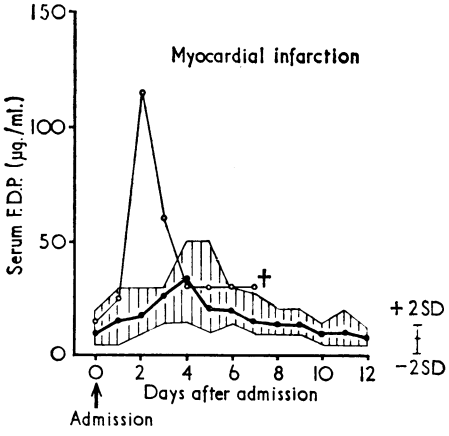

FIG. 2.—The changes in serum F.D.P. in response to acute myocardial infarction in 12 patients. The closed circles represent the mean values of 11 of the patients and the shaded area the range. The open circles are the values obtained from the remaining patient (see text). The mean ±2 S.D. values were obtained from 50 healthy age and sex matched resting controls.

The results from both groups of patients are summarized in Figs. 1 and 2. There was an increase in the mean serum F.D.P. following both abdominal surgery and acute myocardial infarction which was highly significant ($P<0.001$) on days 5 and 7 in the postoperative group and days 3 and 4 in the myocardial infarction group. In three of the 11 surgical patients there was a sudden increase on the third postoperative day which was well outside the range found in the remaining eight patients. Reference to the clinical notes revealed that in one of these patients the diagnosis of pulmonary infarction was made on the same day that a serum F.D.P. value of 336 µg./ml. was recorded. There was no clinical evidence of pulmonary embolus, infarction, or venous thrombosis in the two other patients whose serum F.D.P. peaked during the study. One of the 12 acute myocardial infarction patients also produced a peak of serum F.D.P. without clinical evidence of pulmonary embolus or venous thrombosis. However, during the night on the ninth day after admission he died suddenly and unexpectedly. Necropsy revealed the cause of death to be multiple pulmonary emboli.

It would be premature to conclude from this small pilot study that the quantitative assay of these serum polypeptides will prove to be useful in establishing the diagnosis of suspected or occult pulmonary embolism. There are many other clinical conditions in which disseminated intravascular coagulation and fibrinolysis occur.[4] Moreover, venous thrombosis, without pulmonary embolism or infarction, may have been responsible for some of the serum F.D.P. peaks in the present investigation, although five cases of acute femoral venous thrombosis, without clinical evidence of pulmonary embolus, studied in non-surgical wards, have failed to show serum F.D.P. values above 30 µg./ml. It is also possible that a significant peak in serum F.D.P. is associated with pulmonary embolus only if it proceeds to infarction.

There is no doubt that a major practical problem in any possible future development of this work is the laborious nature of the type of immunoassay used and the duration required (12–24 hours) before a result is available. However, we have evidence to show that the capillary technique of Israels *et al.*[5] can solve the latter problem, and further developments, currently under investigation in this laboratory, may provide an immunoassay which is rapid and simple to execute and perhaps suitable for complete automation.—We are, etc.,

J. D. CASH.
D. G. WOODFIELD.
P. C. DAS.
A. G. E. ALLAN.
South-east Scotland Regional Blood Transfusion Centre,
Royal Infirmary,
Edinburgh.

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Cyclophosphamide and the Nephrotic Syndrome

SIR,—I was interested in your leading article (15 March, p. 660) concerning the use of cyclophosphamide for the treatment of children with the nephrotic syndrome. I noted your omission of reference to our work on this subject,[1] which reached essentially the same conclusions as outlined in your leading article and in the excellent article by Drs. M. W. Moncrieff, R. H. R. White, C. S. Ogg, and J. S. Cameron in the same issue (p. 666).

We believe that the beneficial effect obtained by this drug casts further doubt on the so-called "immunosuppressive" mechanism of action of this agent in this condition, and in fact attests to our ignorance of the mechanism of action of any of these newer drugs in the various forms of glomerular disease. Our subsequent experience with this agent in children with the nephrotic syndrome is similar to that which we originally reported, and it is our opinion that a clear definition of the specific indications for its use is beginning to emerge. We have been concerned by the occasional instances of fatal varicella in children receiving cyclophosphamide for the nephrotic syndrome which have been reported by others, and for this reason we urge the greatest caution in the use of this drug in patients who have not experienced varicella unless it is possible to avoid exposure to this