hyperpyrexia associated with gross muscle rigidity was 54.

Finally, we would like to suggest that all the clinical features of malignant hyperpyrexia might be explained in terms of a single primary event. This primary event could be the continuous presence of excess calcium ions in the myoplasm. This would stimulate and sustain muscle contraction and also activate phosphorylase.[2 3] The latter would keep up the supply of fructose 1, 6-diphosphate for ATP production by glycolysis. Heat would be liberated during the continued synthesis and utilization of ATP and the lactic acid resulting from glycolysis would lead to the severe metabolic acidosis which occurs in malignant hyperpyrexia. The lactic acid would be transported to the blood stream, and in the liver part would be oxidized to provide the ATP necessary for converting the remainder to glucose. These transformations would lead to the liberation of much heat. Glucose synthesized in this way and from liver glycogen might then be transported to the muscle, where the processes activated by calcium ions would be permitted to continue. Liver and muscle mitochondria are both partly uncoupled by halothane and this would further increase heat production. Thus, muscle tissue aided by the liver would operate as a compound ATPase of great magnitude. The primary defect might well be located in that part of the sarcoplasmic reticulum associated with maintaining myoplasmic calcium ions at the level which does not stimulate contraction.—We are, etc.,

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2 Ozawa, E., Hosoi, K., and Ebashi, S., *Journal of Biochemistry*, 1967, 61, 531.
3 Heilmeyer, L. M. G., jun., Meyer, F., Haschke, R. H., and Fischer, E. H., *Journal of Biological Chemistry*, 1970, 245, 6649.

Uterine Hypotonia

SIR,—Further to Mr. H. K. Basu's letter (24 July, p. 251) the theory that uterine hypotonia results from a high level of fibrin degradation products (F.D.P.) leaves some questions unanswered.

Firstly, high levels of F.D.P. are also present in "the 70%" of cases of hypofibrinogenaemia in which postpartum haemorrhage does not occur. In 1969 Mr. Basu wrote[1] that "the occurrence of bleeding is not related to the degree of hypofibrinogenaemia," though it would seem that the level of F.D.P. must be so related.

Secondly, according to Bonnar *et al.*[2] intravenous fibrinogen increases the level of F.D.P., yet to date this is the standard and most effective treatment of hypofibrinogenaemia, though heparin has also been used. In the National Maternity Hospital, Dublin, hypofibrinogenaemia with accidental haemorrhage is commonly encountered, and it has been found to be uniformly responsive to intravenous fibrinogen with adequate blood transfusion.[3] Contrary to current theories no patient suffered ill effects from the treatment. If F.D.P. cause the hypotonia and if intravenous fibrinogen increases their level how does it control the bleeding? Thirdly, patients usually labour well after accidental haemorrhage whether coagulation failure occurs or not.

The suggestion that amniotic fluid causes hypotonia cannot yet be dismissed. Dr. D. F. Hawkins's criticisms (26 December 1970, p. 804) of my experiment (31 October 1970, p. 303) were taken into account. (The uterine muscle was a longitudinal midline fundal strip removed prior to elective caesarean section. Amniotic fluid was aspirated at the same time. The muscle was set up in a 40 ml bath of oxygenated modified Krebs's solution at 37°C, in which a control series had also been done. When the contractions had stabilized after three hours, 5 ml of the amniotic fluid was introduced. Circumstances made it impossible to repeat the experiment.) The histological findings of amniotic fluid in the uterine blood vessels by different workers after hysterectomies for persistent postpartum haemorrhage can hardly be regarded as coincidental.[4-6] It seems clear that in some cases of coagulation failure postpartum hypotonia also occurs. The clinical evidence available is that both uterine hypotonia and coagulation failure are constant features of amniotic fluid infusion.

Last week I had another case of severe postpartum haemorrhage (5 pints; 2·7 l.) following the expulsion of a dead fetus retained in utero for one month. The Lee-White clotting time was 7 minutes, but the clot later partially dissolved, indicating the presence of fibrinogen with active fibrinolysis. The blood issuing per vaginam, however, did not clot, and bleeding continued despite fundal stimulation. The previously described measures (15 May, p. 403) were instituted and trickling continued through the pack. This time Trasylol was available and 200,000 units were given intravenously. The bleeding stopped immediately.—I am, etc.,

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2 Bonnar, J., McNicol, G. P., and Douglas, A. S., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1969, 76, 799.
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Nitroprusside Revisited

SIR,—We were interested to read Dr. M. K. Mani's paper (14 August, p. 407) on the treatment of hypotensive crisis with the rarely used drug sodium nitropruscide. There is no mention, however, of the system of monitoring employed. In our experience with this drug in the production of hypotension during general anaesthesia its potent and evanescent nature makes continuous monitoring of both the infusion rate and the arterial blood pressure mandatory. We recommend the use of an automated drip rate recorder and direct arterial pressure monitoring for this purpose.[1] We think it probable that these safeguards should be employed in the circumstances described in the paper.—We are, etc.,

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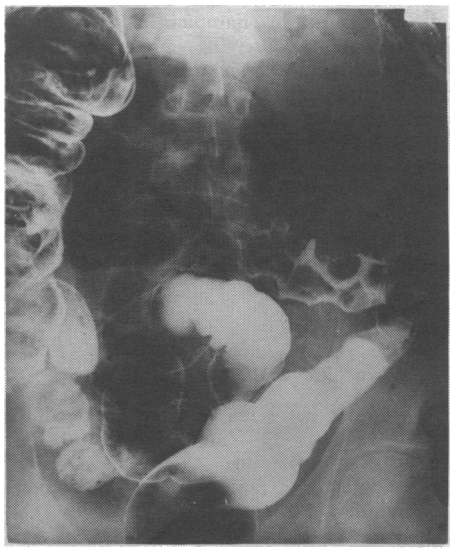
1 Taylor, T. H., Styles, M., and Lamming, A. J., *British Journal of Anaesthesia*, 1970, 42, 859.

Ischaemic Colitis without Predisposing Cause

SIR,—Drs. P. B. Cotton and M. Lea Thomas (3 July, p. 27) describe the association between the syndrome of ischaemic colitis and the taking of oral contraceptives. The following summary describes a patient with ischaemic colitis but without predisposing cause and without occlusion of vessels.

A 37-year-old woman was admitted with a 14-hour history of colicky lower abdominal pain, diarrhoea, and the passage of dark red blood per rectum. She had six to eight bowel actions and the pain was partly relieved by defaecation. She had vomited about six times. There was no significant past history. She had been taking six Veganin tablets (aspirin 250 mg, phenacetin 250 mg, codeine phosphate 10 mg) a day for the last week because of toothache. She was not taking oral contraceptives. On examination she was apprehensive; temperature 38°C, pulse 88, B.P. 130/75. There was tenderness in her lower abdomen and no masses were palpable. Sigmoidoscopy showed that there was blood coming from above the level reached but the mucosa was normal. Barium enema performed next day showed the features of ischaemic colitis between the hepatic flexure and the lower descending colon (Fig.). An abdominal aortogram performed several days later did not show any obstruction in the inferior mesenteric artery system.



The acute episode settled, and she remained well for 12 months, when she began to complain of cramping left-sided abdominal pain associated with defaecation. This pain persisted over the next 12 months when barium enema showed narrowing of the upper part of the descending colon and what appeared to be a cluster of pseudodiverticula in this area.

Laparotomy was undertaken two and a half years after her initial admission. The

colon appeared normal. The only abnormal finding was an adhesion from the greater omentum to the left end of the transverse colon. All vessels were normal and it did not appear that they had ever been occluded.

The ischaemic colitis syndrome exists in the absence of vascular occlusion, and while it is conceded that arterial thrombosis may follow the taking of oral contraceptives care should be taken before attributing a causative role to these drugs, particularly in this syndrome.—We are, etc.,

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Rifampicin and Thrombocytopenia

SIR,—Dr. G. Poole and others (7 August, p. 343) reported the occurrence of thrombocytopenia in patients receiving rifampicin in the dose of 1,200 mg twice weekly.

I have recently seen a patient who developed spontaneous bruising while receiving rifampicin in a dose of 600 mg daily. She had been on rifampicin for about nine months. She was found to have a platelet count of 44,000/mm^3 but no other haematological abnormality. Her antituberculosis chemotherapy was stopped and over the course of the next few days the bruising disappeared. One week later her platelet count was 242,000/mm^3 and has remained normal since.

By the kind co-operation of Dr. Peter Stradling, of the Hammersmith Hospital, the patient's serum was tested and gave no evidence of rifampicin-dependent antibodies by any of the methods described in the report referred to above.

It is not certain that the thrombocytopenia was due to rifampicin as the patient had also been receiving ethambutol and pyrazinamide, but so far as I am aware these drugs have not been reported to cause platelet abnormalities and it may be that clinicians should keep a watch for this potentially serious side effect in patients receiving daily rifampicin also.—I am, etc.,

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Hospital Staff Appointments

SIR,—It does not seem to have occurred to Mr. W. E. Jacobs (14 August, p. 435) that if one is job-hunting one may need to apply for several posts simultaneously, and that the interview for the job one really wants may come after that for one which is inferior. It takes a certain amount of cash in the bank or a lot of confidence to withdraw from the first interview in the hope of success in the later one. It could even be that the job at his hospital isn't quite as attractive as he thinks it is. There is a lot to be said for consultants and hospitals having to provide references by previous holders of the post advertised.

The *Hospital Gazetteer* is rather less useful than the A.A. hotel guide; what is really needed is a register as candid and hard-hitting as a *Which?* report.

When I was last job-hunting, I drew up forms asking for what I felt was the most relevant information about the job and accommodation offered, which I sent to the hospitals with my applications. This obviously startled many of the recipients, but it did save me some wasted journeys—including the one or two who did not feel it was necessary to reply until the interview. Obviously any consultant or administrator who takes this attitude is unlikely to be a congenial person to work with, and frankly they don't deserve to have any junior staff.

One other point that could be mentioned, which causes considerable resentment, is the "rigged" appointment. Please note I am *not* complaining about hospitals appointing someone whom they already know; I think it is usually much more satisfactory for all concerned if the person known and liked locally gets the job, and if one has held a post satisfactorily as a locum, then one darn well should get it. What I do think is wrong is to call candidates from all over the country just to put on a show of "fairness;" actually it is very unfair to the other candidates, whose hopes are raised unnecessarily, whose time is wasted, who may miss another interview where they might have been successful, and who invariably end up out of pocket as the subsistence rates paid are completely out of touch with present costs of hotels and restaurants. Furthermore, some regional boards will not pay expenses for visiting the hospitals prior to interview, though this is a sensible precaution (for both sides), particularly where the post is one to be held for more than a few months, and if candidates were encouraged to do this there might be fewer late withdrawals.—I am, etc.,

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SIR,—While agreeing with Mr. W. E. Jacobs (14 August, p. 435) that it is very wrong for hospital junior doctors to accept posts and then turn them down at a later date, I feel the hospitals themselves are partly to blame for the following reasons.

Posts are usually advertised only a few weeks before the job is due to start. So many doctors approaching the end of their contract have no new post to go to. They are then tempted to accept a post they do not like in order to give their family a home. Subsequently, when offered a job they do like they turn the first job down. This applies particularly to foreign doctors with no relatives to impose upon.

Insufficient information about posts is usually given before interview. A candidate may accept the post before he has had sufficient time to consider the disadvantages such as poor accommodation, no postgraduate facilities, poor library, night cover for other specialties, and poor off duty.

Contracts for hospital junior staff are extremely short—a problem faced by no other employee of the N.H.S. Two-year rotating appointments with some thought for the training needs of the young doctor would reduce the turnover of staff and also reduce the difficulties encountered by the hospitals and the doctors.

If any job is continually being turned down by candidates after interview the job itself should be investigated. Better training facilities and conditions of work may produce a suitable doctor.—I am, etc.,

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Thromboplastin Reference Preparations

SIR,—The statement by Drs. Rosemary Biggs and D. R. Bangham (21 August, p. 470) represents the culmination of several years study by the Thromboplastin Subcommittee of the International Committee for Haemostasis and Thrombosis, with which I and many others have been associated. It is therefore a landmark in the development of stable international reference preparations for thromboplastin.

It is important, however, to emphasize several points lest there be confusion in British hospitals regarding the implications of their statement as we already have a nationally adopted scheme for anticoagulant control. It should first be mentioned that one of these proposed international reference preparations (Thromboplastin 1 (69/223) plain) is in fact a special batch of material provided from Manchester which had been processed in a similar way to the British Comparative Thromboplastin. It is in fact identical with the B.C.T. for the purposes of anticoagulant control, provided that the proposed reference preparation (69/223) remains stable. The properties of the B.C.T. are in all events well established in clinical practice, whereas the other reference reagents are unknown quantities in terms of treatment ranges and could not be used with the same degree of confidence.

The thromboplastin sensitivity ratio[1] advocated in the statement is completely different from our nationally adopted system for reporting prothrombin results using the British Corrected Ratio and the two must be distinguished. The method of obtaining the B.C.R. has been explained in detail in an A.C.P. Broadsheet and elsewhere.[2-4]

As the statement says, the proposed use of thromboplastin reference preparations is for the characterization of national reference preparations and not for use as working reference reagents in hospitals. The only snag is that to date there is only one national reference reagent—that is, the British Comparative Thromboplastin, and the character of this is far better established than that of any of the reference preparations. Its quality control at the production centre, at the expert monitoring laboratories, and via the independent assessor is far stricter than any other thromboplastin. If therefore these reference preparations are to be of clinical value there must be development of national systems of anticoagulant control, perhaps similar to the British system, in order to provide working reference reagents for individual hospitals and for commercial manufacturers.—I am, etc.,

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2 Poller, L., *Association of Clinical Pathologists Broadsheet*, 1970, No. 71.
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4 Thomson, Jean M., *A Practical Guide to Blood Coagulation and Haemostasis*, p. 172. Churchill, London, 1970.