attempting to cope with too great numbers during panic procedures. I regard my suggestion as a minimal safeguard for doctors, nurses, and patients involved in immunization procedure.—I am, etc.,

GUY BOUSFIELD

Warnham,
Horsham, Sussex

Co-trimoxazole Resistance

SIR,—The letter from Drs. R. Then and P. Angehrn (12 January, p. 78) requires comment. The first point raised in this letter concerns our use of Oxoid nutrient broth no. 2 for determining bactericidal effect. We did in fact use this broth with the addition of 5% lysed horse red cells, and said so in our letter (20 October, p. 165). This medium has been used successfully for many years for testing the activity of sulphonamides and trimethoprim in vitro; its suitability results from the release of an enzyme, thymidine phosphorylase, that converts free thymidine to a derivative with a much reduced antagonistic potential.[1] Our first point was that *even* in this medium the bactericidal action of trimethoprim/sulphamethoxazole mixture is uncertain;[2] any bactericidal action is due to the presence of the trimethoprim component alone.[3]

In the remainder of their letter Drs. Then and Angehrn speculate about the amount and significance of free thymidine in human tissues. They concede that "there are only a few data published on the thymidine content of human tissues"; our second point was that there must be some thymidine present, and its level may well be sufficient to jeopardize any bactericidal action of co-trimoxazole in vivo.—We are, etc.,

R. W. LACEY
EVELYN L. LEWIS

Bristol Children's Hospital,
Bristol

1 Bushby, S. R. M., *Medical Journal of Australia*, 1973, **1**, Special Suppl., 30 June, p. 10.
2 Lewis, E. J., and Lacey, R. W., *Journal of Clinical Pathology*, 1973, **26**, 175.
3 Lacey, R. W., Anderson, J. D., Lewis, E. L., and Gillespie, W. A., *Lancet*, 1973, **2**, 509.

SIR,—In their interesting letter Dr. R. Then and P. Angehrn (12 January, p. 78) conclude that co-trimoxazole-resistant thymine- or thymidine-dependent bacterial mutants are rare and of little clinical importance, but add that many may have been overlooked. Hutchison and his colleagues have studied a number of such strains.[1 2] We reported the isolation of such an *Escherichia coli* mutant in this laboratory in pure culture from a surgical wound.[3] The patient had not been treated with co-trimoxazole. The organism thrived on blood agar but failed to grow on lysed blood agar used for sulphonamide sensitivity testing, this practical problem being overcome by sensitivity testing on Oxoid Sensitest medium. We have since recognized that occasional mucoid strains of coliform bacilli showing co-trimoxazole resistance have rather similar peculiar growth characteristics. A recent isolate from the urine of a patient who did not respond to co-trimoxazole was difficult to study in the state in which it was isolated because it so rapidly reverted to normal growth in vitro though remaining resistant to co-trimoxazole. It appears then that such strains can be found from time to time in primary cultures if they are looked for, and do not necessarily appear only in patients who have previously received co-trimoxazole.—We are, etc.,

MAIR THOMAS
MARIA DZIEJKO

Bacteriology Department,
Elizabeth Garrett Anderson Hospital,
London N.W.1

1 McGhie, D., Hutchison, J. G. P., and Finch, R. G., *Journal of Clinical Pathology*, 1972, **25**, 976.
2 Barker, J., Healing, D., and Hutchison, J. G. P., *Journal of Clinical Pathology*, 1972, **25**, 1086.
3 Thomas, M., and Bond, L., *Medical Laboratory Technology*, 1973, **30**, 277.

Complication of Laparoscopy during Early Pregnancy

SIR,—We would like to report a potentially serious complication of laparoscopy (lower abdominal peritoneoscopy). We believe that insufflation of carbon dioxide into the uterine cavity is particularly likely to occur in patients who have just had a pregnancy terminated and that this is very likely to lead to hypotension or cardiac arrest, possibly due to gas embolism.

To support this, we report the cases of three patients in whom vaginal termination of a 12-14-week pregnancy was followed immediately by laparoscopy for sterilization. All had 0·5 mg of ergometrine given intravenously before termination. Laparoscopy was performed under general anaesthesia with the patient paralysed, hyperventilated, and in the steep Trendelenburg position. A Verres's needle was inserted at the junction of the upper and middle thirds of a line from the umbilicus to the symphysis pubis (so avoiding the aortic bifurcation) and was directed towards the lower end of the sacrum. Carbon dioxide was insufflated at the rate of 1-2 l./min and the pressure was continuously monitored and never allowed to exceed 30 mm Hg. The laparoscopies were done by different surgeons, each of whom had experience of over 200 laparoscopies.

In the first case, 30-40 seconds after the insufflation of the carbon dioxide had started gas was seen escaping through the cervical os. The needle was immediately withdrawn. At the same time the patient became pulseless and cyanosed, with dilated pupils. Resuscitative measures promptly restored her circulation to normal. She made an uneventful and complete recovery. In the second case, after 20-30 seconds of insufflation gas was seen escaping through the cervical os and the needle was immediately withdrawn. Her systolic blood pressure fell to below 60 mm Hg for about five minutes and then returned to normal without any specific treatment. In the third case, after less than 20 seconds of insufflation gas was seen escaping through the cervical os and the needle was immediately withdrawn. There was no recorded change in her blood pressure.

We believe the cause of the cardiac arrest in the first case and hypotension in the second may have been gas embolism. Carbon dioxide is commonly used for tubal insufflation in non-pregnant patients without causing gas embolism. However, it is well recognized that air can enter the open and dilated sinuses of the uterus immediately after delivery and cause air embolism. In these three patients, the soft pregnant uterus and the enlarged, empty uterine cavity would explain why the Verres's needle was so easily inserted into the uterine cavity. The raw surface of the uterine cavity immediately after the termination might well have allowed ready passage of the carbon dioxide into the blood stream.

We suggest that in patients who have undergone termination of pregnancy the uterus should be depressed into the hollow of the sacrum (for example, with a Currie's cannula) during the insertion of the Verres's needle; and that during the insufflation of carbon dioxide a careful watch should be maintained for gas escaping through the cervical os and frequent measurements of the blood pressure taken.—We are, etc.,

M. B. BARNETT

Department of Anaesthetics,
Royal Sussex County Hospital

DAVID T. Y. LIU

Brighton
University of Sussex.

Effects of Oral Contraceptives on Endogenous Hormone Secretion

SIR,—The findings of Dr. Max Elstein and his colleagues (5 January, p. 11) were of great interest to us as we too have been studying endogenous hormone secretion in women during treatment with oral contraceptives of similar composition. We were particularly struck by the remarkable lack of suppression of luteinizing hormone (LH) excretion during the treatment cycles studied by Dr. Elstein and his colleagues. We have measured serum LH and follicle-stimulating hormone (FSH) by radioimmunoassay and compared basal levels and the response to gonadotrophin-releasing hormone (Hoechst) in normal women during the luteal phase with those observed in subjects during the third week of a treatment cycle with a combined oral contraceptive (containing 50 μg ethynyl oestradiol and 1-2 mg progestogen). In the subjects taking the oral contraceptive we found lower basal concentrations of LH and FSH and an impaired response of the gonadotrophins to the releasing hormone.[1]

There appear to be two major differences in experimental design which might account for the difference in results. Whereas we studied subjects after about a year's treatment, Dr. Elstein and his colleagues studied the first two cycles after starting therapy. However, it seems unlikely to us that the pattern of hormone secretion would radically change after a year's treatment and we think a more likely cause relates to the method of assessment of gonadotrophin production. Dr. Elstein and his colleagues measured urine excretion of LH by radioimmunoassay, an approach which is subject to such a large number of problems[2] that some workers, on the basis of extensive comparative studies[3] have concluded that the radioimmunoassay of LH in unextracted urine is invalid.[4] It would therefore be of great interest to know whether the measurements of LH excretion described by Dr. Elstein and his colleagues were obtained—as suggested by their method reference—on unprocessed urine. If the urine was processed before assay, which method was used? The point is of more than methodological interest, since the two sets of results imply quite different mechanisms of action of the oral contraceptives.—We are, etc.,

HOWARD JACOBS
ANNE M. JEQUIER

Middlesex Hospital and Institute of Nuclear Medicine,
London W.1

1 Jequier, A. M., *et al.*, *Journal of Endocrinology*. In press.
2 Jacobs, H. S., and Lawton, N. F., *British Medical Bulletin*, 1974, **30**, 55.
3 Stevens, V. C., *Journal of Clinical Endocrinology and Metabolism*, 1969, **29**, 904.
4 Stevens, V. C., *Acta endocrinologica*, 1969, **63**, Suppl. no 142, p. 338.