Based on many years of preliminary work and experience FRAME (Fund for the Replacement of Animals in Medical Experiments) already has an active centre at which information is collated from world-wide published data and from direct contact with scientists. The information is disseminated widely among many individuals and teams who are concerned with developing advanced multidisciplinary techniques in medical research. Some time ago proposals were submitted by FRAME to both the United Kingdom Government and the Council of Europe stressing the need for a documentation centre.

The Medical Research Council and equivalent bodies elsewhere who necessarily use animals at present are already extensively backing work in several fields aimed at minimizing many animal tests and their accompanying problems. It is our firm conviction that it is a waste of time and money to duplicate existing research work and to set up costly new establishments. What is essential is the interchange of information about alternatives, and the encouragement of people now working in many centres to co-operate with others in developing acceptable replacement techniques. Some of the most interesting advances are stemming from those who use animals at present.

In your leading article "Animal Experiments" (25 December 1971, p. 762) it was stated that the Council of Europe's Recommendations 621 (1971) were unfavourably received by the World Medical Association. FRAME contends that had the proposals for a documentation centre been separated from the activities that are primarily concerned with control of animal usage, strong support for the centre may well have resulted. Information and education are not contentious issues and can be supported by all through the FRAME Centre.—I am, etc.,

C. E. FOISTER

Chief Scientific Adviser, FRAME

London S.W.20

The Red Cell

SIR,—Dr. D. A. T. Dick (26 February, p. 571) is right in stating that intracellular and extracellular fluids have the same osmotic pressure, and his views on the role of haemoglobin are essentially correct.

The movement of water through the red cell membrane is, as I have stated, not a matter of simple osmosis. Sodium ions enter and potassium ions leave the cell by passive diffusion. Sodium ions are "pumped" from the cell against an electrochemical potential gradient, a process which requires the expenditure of energy. Potassium ions enter the cell by a similar mechanism. The red cell is ceaselessly engaged in balancing the pump and the leak.—I am, etc.,

G. W. G. BIRD

Regional Blood Transfusion Service,
Birmingham

Prostaglandin-oxytocin Enhancement

SIR,—Dr. Arnold Gillespie (15 January, p. 150) indicates that uterine contractions can be enhanced if oxytocin is given after previous exposure to prostaglandin E₂.

Brummer¹ showed by in vitro experiments that after exposure to the E₂, but not to the F_{2α} prostaglandins (PGF_{2α}), human myometrial strips exhibited an enhanced response to oxytocin. We report here preliminary results on the abortifacient effect of a combined treatment with PGF_{2α} and oxytocin.

The combined treatment, administered extra-amniotically by means of a Foley catheter introduced between the fetal membranes and the uterine wall through the cervical canal, was given to 32 women admitted to hospital for termination of mid-trimester pregnancies. A dose of 0.5 mg PGF_{2α} (Astra) was given hourly to 20 women. Higher doses (0.75–2.0 mg) were used if the uterine contractions were weak or lacking. Nine women received a mixture containing 0.5 mg of PGF_{2α} and 1 I.U. of oxytocin, and three women received 3 I.U. of oxytocin alone. The results are shown in the Table.

	PGF _{2α}	PGF _{2α} +Oxytocin	Oxytocin
No. of cases	20	9	3
Complete abortions	7	5	—
Incomplete abortions	10	4	1
Failures	3	—	2
Average abortifacient dose	26.1 mg	15.2 mg 30.4 I.U.	108 I.U.

In the PGF_{2α}-group of 20 patients abortion was complete in seven and incomplete in 10 cases. Three failures were encountered. The trial was considered as a failure if uterine contractions stopped in spite of continuous and increased dosage. In the group of nine women having a mixture of PGF_{2α} and oxytocin there was no failure. Abortion was complete in five and incomplete in four cases. Of the three women who received oxytocin only, one aborted and two failed. Uterine contractions were present in all three cases.

The mean dose of PGF_{2α} required for an abortion was 26.1 mg in the prostaglandin group, while that in the combined PGF_{2α} and oxytocin group was 15.2 mg. Two out of the three failures in the prostaglandin group could be successfully treated with an intravenous oxytocin infusion (5 I.U./hour, which caused uterine contractions when prostaglandin had no more effect. Hysterotomy was needed in one case, where a bicornuate uterus was found at the operation. Extra-amniotic oxytocin alone caused uterine contractions in all three cases included in the trial, though abortion was achieved in only one. The two failures in the oxytocin group were treated with extra-amniotic prostaglandin. In the total series of 32 cases, hysterotomy was not required in 31 (97%) if both prostaglandin and oxytocin were used.

PGF_{2α} and oxytocin have a contractile effect on the uterus in vivo during the mid-trimester. Whether the effects of these two drugs are additive or potentiative is being studied.—We are, etc.,

M. SEPPÄLÄ
P. VARA

Department II of Obstetrics and Gynaecology,
University Central Hospital,
Helsinki, Finland

¹ Brummer, H. C., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1971, 78, 305.

Do-it-yourself Pregnancy Test

SIR,—Early in 1971 we agreed to investigate the reliability of the Twentisecc chemical test for pregnancy, described as being suitable for self-use by the patient. In the test two drops of the reagent, a halogenated cresol derivative, are mixed with a given quantity of the patient's urine and the resultant colour compared against a white background with a colour chart. When positive the colour changes from light reddish purple to deep purple, and when negative it is yellow or light brown.

Samples of first morning specimens of urine were obtained from patients attending the antenatal clinic, and they provided further samples weekly. Negative control specimens were obtained from patients known not to be pregnant, and to us they were indistinguishable from specimens obtained from the clinic. All the patients and controls were told about the trial and reminded of the manufacturer's instructions that only first specimens of urine passed in the morning should be used and that no food or drugs should be taken for 10 hours before the test. All the tests were done within eight hours of the urine being passed and put into clean, dry, specimen bottles provided. The control specimens were from patients not on oral contraceptives or other hormones, since these might cause false positive results. In this part of the series 74 patients (including negative controls) provided 189 specimens.

The influence of menopausal gonadotrophin was studied by testing urine from 25 postmenopausal women in general medical wards. A further 48 random samples of urine submitted to the laboratory for pregnancy testing were also examined.

All the samples were tested by one of us (A.W.C.), who observed in detail the manufacturer's instructions for carrying out the tests. As a comparison, all the samples were also tested by the standard Pregnosticon technique currently used as the routine method of pregnancy testing in the laboratory.

Of 133 samples from patients subsequently shown to have been pregnant at the time all were positive to the Pregnosticon test while only 87 were positive by the Twentisecc method (that is, 35% false negatives). Pregnosticon testing of the 56 negative control samples gave 55 negative and one doubtful positive, whereas the Twentisecc test gave 38 negative and 18 positive results (that is, 32% false positives). The samples from the 25 postmenopausal patients were negative to Pregnosticon testing in all cases but the Twentisecc test on the same samples gave positive readings in 12 cases (48% error).

During the period of study we tested by both methods 48 early-morning urine specimens submitted in the normal manner. The tests gave similar results in only 26 cases. In the remainder the Twentisecc was negative in 12 in which the Pregnosticon test was positive, and positive in eight in which the Pregnosticon test was negative. In two doubtful positive results by Pregnosticon testing the Twentisecc test was negative.

The pH of all samples of urine from pregnant patients was estimated, and it was noted that the mean pH of those giving positive results with both Twentisecc and Pregnosticon was 6.83. For the samples giving false negative results on Twentisecc testing the mean pH was only 6.01. We have since heard from the manufacturers that the main ingredient of the chemical used in the test is bromocresol purple, which explains why there is apparently a pH effect. Further testing in our laboratories has shown that positive results can be made negative by acidifying the urine and conversely any urine

can be made to give a positive result by making it alkaline.

Our study shows that even carried out in ideal laboratory conditions the Twentisecc test is too inaccurate to be used in its present form even as a screening test. Since we completed our study and from knowledge of the results the manufacturers have been advised to withdraw Twentisecc test kits from the market.¹

We wish to acknowledge the co-operation of Mr. S. Gee and Global Laboratories (Universal) Ltd., who generously supplied the Twentisecc test kits used in the study, and to thank the nursing staff of the antenatal clinic at University College Hospital Obstetric Hospital for their help in organizing the survey. We are also grateful to Dr. Joan Stokes for advice and encouragement.

—We are, etc.,

D. V. I. FAIRWEATHER
A. W. CREMER

University College Hospital Medical School,
Obstetric Hospital,
London W.C.1

¹ Winstanley, M., *World Medicine*, 1971, 7, 9.

Neonatal Meningococcal Conjunctivitis

SIR,—Severe purulent conjunctivitis in newborn infants (ophthalmia neonatorum) is usually caused by TRIC agent^{1,2} or by *Neisseria gonorrhoeae*.^{3,4} However, thorough bacteriological examination of such cases is important, as the following report indicates.

A healthy baby, whose mother was Greek, developed severe conjunctivitis on 25 May 1970 at the age of five days. The conjunctivitis affected the right eye, which showed lid oedema, purulent exudate, and chemosis. Culture of pus yielded an abundant growth of *Neisseria meningitidis* in pure culture. Conjunctival smears stained with Giemsa revealed abundant neutrophils and intracellular diplococci; TRIS agent inclusion bodies within epithelial cells were not detected. The meningococcus fermented glucose and maltose but not sucrose. Agglutination tests with meningococcal group C sera (Burroughs Wellcome, Commonwealth Serum Laboratories) yielded positive results. When tested by the disc diffusion method on heated blood agar, the meningococcus was sensitive to sulphadiazine (25 micrograms (μ g) per disc), sulphadimidine (25 μ g), sulphamethoxazole (25 μ g), penicillin (0.6 μ g = 1 unit), ampicillin (2 μ g), tetracycline (10 μ g), chloramphenicol (10 μ g), and erythromycin (2 μ g). By the plate titration method, using horse blood agar and Mueller-Hinton medium with 5% horse serum, respectively, the minimal inhibitory concentration of penicillin G was 0.05 μ g per ml (= 0.08 units per ml) and of sulphadiazine 0.2 μ g per ml (0.02 mg per 100 ml).

The conjunctivitis was treated by the instillation of chloramphenicol drops and this resulted in clinical improvement and bacteriological cure. However, on the following day, 26 May, the infant showed mucopurulent nasal discharge, and culture of this exudate yielded abundant growth of a meningococcus, also sensitive to penicillin and other antibiotics. Oral penicillin was consequently administered.

The source of infection was not established in this case. It was considered that infection probably originated from a meningococcal carrier, either the baby's mother or a member of the attendant hospital staff. Because of suspected endometritis the mother had been treated with ampicillin

after delivery; culture of cervical and urethral swabs collected subsequently failed to yield *Neisseria*.

As the work of C. Brons⁵ and R. D. Stuart⁶ showed, meningococcal conjunctivitis occurs in infancy and childhood and may readily be confused with gonococcal infection, as such cases cannot be distinguished clinically. Unless cultures are made and the identity of the isolate established, a false diagnosis of gonococcal conjunctivitis may be made. An unusual feature of the present case was the early age of onset, as we know of no fully documented report of meningococcal conjunctivitis in the first four weeks of life.—I am, etc.,

D. HANSMAN

Pathology Department,
Women's Hospital,
Sydney, N.S.W., Australia

¹ Watson, P. G., and Gairdner, D., *British Medical Journal*, 1968, 3, 527.

² Hansman, D., *Medical Journal of Australia*, 1969, 1, 151.

³ Smith, J. A., *Scottish Medical Journal*, 1969, 14, 272.

⁴ *Lancet*, 1969, 2, 630.

⁵ Brons, C., *Zentralblatt für Bakteriologie* 1909, 48, 141.

⁶ Stuart, R. D., and McWalter, D., *Lancet*, 1948, 1, 246.

Obesity

SIR,—The article on obesity (26 February, p. 560) added little if anything to the armamentarium of the average general practitioner, and contained two unfortunate statements. Most general practitioners would not agree that there are more young men than women who are significantly overweight, and in the freshmen at this University the ratio of overweight men to women is 1:3.

The inclusion of apples in the list of otherwise recognized fattening foods (for example bread and potatoes) in the sentence on 100 kcal sources may make the unsuspecting wonder whether fresh fruit may freely be allowed to those on a reducing diet after all. It would have to be a truly enormous eating apple to supply this number of calories—500 g or more. Life is hard enough for the slimmer (and her doctor) without implying that she can't eat freely of fresh fruit.

Since obesity is such an important and frequent problem—one in ten of the freshmen here are significantly overweight—it is important that its management is correctly based.—I am, etc.,

T. C. DANN

University of Warwick

SIR,—In his article on "Obesity" Dr. John Anderson (26 February, p. 560) advises weighing once a week or a fortnight. In premenopausal women mid-cycle weights are usually preferable. This minimizes misleading—and sometimes discouraging—results due to cyclical fluid retention.—I am, etc.,

JEFFREY SEGALL

London N.W.2

Disodium Cromoglycate in Young Children

SIR,—We have been surprised to find in current literature¹ and be told repeatedly by doctors inside and outside hospital that asthmatic children under the age of 6 or 7 years are rarely able to co-operate in inhaling disodium cromoglycate (Intal).

Among 200 children with asthma attending a special paediatric clinic in this hospital, 41 began successfully to take Intal before their fifth birthday. Of these, six started treatment before the age of three (youngest aged 2 years 4 months), and 10 others before the age of four.

We believe that failure of the young child to use a Spinhaler is probably due to a lack of detailed explanation and instruction in the working of the apparatus to both the child and the parent. These must be supplemented by frequent and continuous encouragement and support.

We feel it is unfortunate that this myth should be perpetuated and thus deny the young asthmatic child a chance to benefit from simple and proven efficient treatment.—We are, etc.,

S. BEDFORD
J. A. KUZEMKO

Peterborough District Hospital

¹ *Disodium Chromoglycate in Allergic Airways Disease*, proceedings of a symposium at the Royal Society of Medicine, ed. J. Pepys and A. W. Frankland. London, Butterworths, 1969.

Gynaecological Illness after Sterilization

SIR,—May I add a cautionary word to your recent correspondence (19 February, p. 504) on the merits of total vaginal hysterectomy as a sterilization procedure? I have within six weeks met two patients who suffered loss of orgasm following this procedure. Both had previously rich sexual lives; both approached surgery confident in assurances that this would be unimpaired. In neither was an unconscious need for the possibility of further pregnancy a relevant factor.

A woman of 51 had vaginal hysterectomy for menorrhagia four years ago. The first post-operative intercourse, eagerly anticipated, was a deep disappointment and shock to her and her husband. It took them two years to relearn a technique satisfactory to them both. The emotional trauma for both was severe; it is unlikely that a less rich and stable relationship would have survived it.

A woman of 47 had the operation for the same reason three years ago, and complained of "frigidity" since. Attempts at intercourse produced no orgasm for 18 months and were abandoned. Great marital stress has resulted. Armed with the knowledge of the preceding patient, I could interpret the anxiety and despair, and recommend a re-educative technique.

Rationally advisable though it may be, the loss of her child-bearing apparatus has always potentially profound psychological implications for a woman. If her fears about loss of femininity are not to become fact, it seems important to elicit pre-operatively how important is cervical and uterine sensation to her sexual performance. Prophylactic re-education may then begin in good time. Her sexual capacity need not be diminished, but the couple are entitled to be warned that their sensation may be different.—I am, etc.,

PRUDENCE TUNNADINE

London W.1

SIR,—Though I have read Professor J. S. Scott's letter (19 February, p. 504) carefully several times I still find his logic questionable and his claims difficult to accept. The thesis that many women who are sterilized are best treated by hysterectomy is now