positive results and false security to those with false-negative results. This would soon lead to possible disrepute and abandonment of what may with proper evaluation and refinement prove to be a most useful addition to antenatal care.—We are, etc.,

G. M. ADDISON
K. T. EVANS
BRYAN HIBBARD
K. M. LAURENCE
C. R. LOWE
C. J. ROBERTS

Welsh National School of Medicine,
Cardiff

Alternatives to the Fluoridation of Water

SIR,—I was very disturbed by your leading article (8 March, p. 535). Though the opening sentence states that fluoridation of drinking water is "the most effective and practicable means of reducing dental caries," the remainder of the article manages to convey the impression that alternative methods of using fluorides might be almost as effective. This is extremely doubtful.

Estimates of caries prevention for a given method of prophylaxis are mainly based on short-term clinical trials. It is then commonly assumed that the percentage reduction observed over the period of the trial will apply throughout life. Such assumptions stem from an imperfect understanding of the natural history of dental caries. In many persons the first attack of dental caries occurs shortly after the eruption of deciduous teeth. Further attacks may then occur on the deciduous and then the permanent dentition throughout life, though attacks become very infrequent beyond the age of 40. The estimated average "ceiling" level of caries in English non-fluoride communities is about 24 attacked teeth, comprising seven deciduous and 17 permanent teeth. Genuine primary prevention of caries requires that this ceiling level of attack should be reduced permanently.

It is often claimed that fluoride dentifrices can reduce caries by up to 30%. The type of trial from which such claims are made is typically of three years' duration, involving children from the age of 11 through to 14. The normal increment of attacked teeth from 11 to 14 years of age is about three, and an average reduction of about one may be observed in treated populations. However, what happens after the age of 14 is unknown. The benefits of fluoridation of drinking water tend to fade with increasing age (though there is a substantial residuum of true primary prevention) and it seems likely that even if fluoride dentifrices, for example, are used throughout life the benefits observed during a short-term clinical trial will also fade. For all we know they might fade to zero.

Similar criticisms can be extended to those conclusions that have been drawn from trials of fluoride rinses, the topical application of fluoride, fluoridated school milk, and fluoridated drinking water in schools. Whereas the life-long benefits of fluoridation of drinking water are well established, those for alternative methods remain largely conjectural.

Some practical difficulties associated with these alternatives should also be emphasized. Whenever a public health scheme has involved the distribution of fluoride tablets it

has had to be rapidly terminated because of lack of parental co-operation. Better discipline could probably be achieved in schools, but the problem of providing fluoride tablets to each child, every day, in every school, is so daunting that the efficacy of the method must be doubted. The same objections can be raised against the introduction in schools of fortnightly rinses with fluoride solutions. Costs are an important consideration these days. According to one estimate fluoride rinses would cost £4 per child per year. For 10m. children the costs would therefore be some £40m. per year, whereas fluoridation of the entire drinking water supplies in Britain would cost about £2.5m. per year.

In terms of economy, convenience, and efficacy the fluoridation of water supplies enjoys immense advantages; it has no serious rivals.—I am, etc.,

D. JACKSON

University Department of Child
Dental Health,
Leeds

Induction of Labour and Perinatal Mortality

SIR,—Termination of pregnancy is a positive contributing factor to dramatic falls in perinatal mortality (Mr. R. H. Tipton and Mr. B. V. Lewis, 15 February, p. 391). British^{1,2} and American³ experience reveals the close correlation existing between certain maternal factors and a high perinatal mortality. The groups in which high rates are found include those of low socioeconomic status, young women and those over 35 years of age, those receiving inadequate antenatal care, and the unmarried. In this last group Crellin⁴ showed a 32% higher perinatal mortality rate than the average and a high number of low birth weights and dysmature infants.

The sociological characteristics of women presenting for termination are similar to those associated with increased perinatal mortality. The number of social class 4 and 5 women in Beard's⁵ termination clinic was nearly double that expected and 56% were single. Seventeen per cent. of all women undergoing termination in England and Wales in 1971 were over 35 years of age.⁶ It is therefore not surprising that a fall in perinatal mortality should occur as a result of the temporary exclusion from reproduction of women and girls who contribute disproportionately to this rate. Rovinsky⁷ in New York reported significant falls within two years of the introduction of an extremely liberal abortion programme in the rates for perinatal mortality (29%), maternal mortality (28%), prematurity, spontaneous miscarriage, and delivery with inadequate antenatal care. The increasing use of sterilization is another contributing factor to this fall. It further removes from future "poor" reproduction the young and grand multipara and women with recurring unsatisfactory obstetric performance.

Liberal sterilization and abortion policies may, as well as reducing perinatal mortality, influence the present alarming escalation in juvenile crime. It is estimated that 5000 hardened criminals under age 15 exist in London alone. Sociologists^{8,9} studying the family backgrounds of these young offenders conclude that many of their mothers possess the behavioural and cultural characteristics mentioned above in relation to perinatal mortality. These mothers constitute an in-

creasing proportion of applicants for sterilization and termination^{5,6}—that is, young unmarried and "older" multiparous women. In the Magdalen Approved Schools⁹ 23% of young women were illegitimate, two-thirds lived with only one parent, and a staggering 38% had some definite evidence of maternal deprivation. Nearly two-thirds of mothers of illegitimate children have full-time jobs during the child's pre-school years, while the illegitimate child faces frequent changes of home and subjection to overcrowding and is stifled in its intellectual and social attainments.¹⁰ Is it any surprise that delinquency and crime result?

It can be no great intellectual revelation that children born illegitimate, from large families, and of mothers refused termination¹¹ make up a large proportion of today's juvenile and adolescent delinquents.^{9,11} One can only speculate that with curtailment of fecundity in some of these married and unmarried mothers a decrease in or stabilization of the present daunting situation à propos juvenile crime may occur.—We are, etc.,

ALBERT SINGER
IAN D. COOKE

University Department of Obstetrics and Gynaecology,
Jessop Hospital for Women,
Sheffield

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Dangers of Silent Gall Stones

SIR,—The logic of your leading article (22 February, p. 415) is open to criticism. It is true that about 1000 out of 100 000 malignancy deaths per year are ascribed to the gall bladder and biliary passages. Of these the Registrar General¹ tabulates 183 as occurring below the age of 60, 91 in men and 92 in women. As the incidence of gall stones in women is twice that in men it is at least possible that the association between stones and malignancy is not a causal one.

In 1965 some 250 000 men in England and Wales reached their 60th birthday. Let us assume that half of those going to develop gall stones are recognized and that 25 000 or 10% have a cholecystectomy, with 360 postoperative deaths. Instead of 21 860 of these 25 000 reaching their 65th birthday (Registrar General's Life Tables, 1965¹) 21 500+100 lives saved will survive so that there is a net loss of about 1% of lives. In subsequent decades, possibly less valuable as regards the enjoyment of life, the balance

may slowly be redressed; but so long as deaths from all forms of gall bladder disease are less than 3 per 1000 deaths from all causes it is difficult to justify a theoretical operation rate of 200 per 1000 with a 1½% operation mortality giving us the same three deaths per 1000 as without operation. I have chosen the most favourable assumptions. It is not unlikely that the expectation of life of patients with gall stones is reduced whether or not they survive cholecystectomy.—I am, etc.,

DENYS JENNINGS

Budleigh Salterton,
Devon

1 Registrar General's Statistical Review for England and Wales 1965, pt. I Tables, Medical. London, H.M.S.O., 1967.

Reactions to Practolol

SIR,—In view of the recent reports of reactions to practolol, possibly on an auto-immune basis, we were interested to observe what we believe to be the first case of practolol-induced "shoulder-hand" syndrome.

A 64-year-old woman with ischaemic heart disease and myxoedema was admitted with angina. She had been treated for two years with practolol, bendrofluazide, slow-release potassium, digoxin, glyceryl trinitrate, doxepin, and thyroxine. Eight days after admission she developed symmetrical, hot, painful swelling of both hands. Practolol was stopped and the symptoms and signs regressed over three days. Reintroduction of practolol 10 days later was associated with reappearance of the signs and symptoms within 72 hours. These again regressed when the practolol stopped five days later.

Antinuclear antibodies were present in high titre but organ-specific antibodies were negative. We also noted that the serum alkaline phosphatase, aspartate aminotransferase, γ -glutamyl transpeptidase, and bilirubin levels rose during the acute attack and are now normal.—We are, etc.,

W. A. STUBBS
M. B. ABLETT

Cardiovascular Unit,
Hammersmith Hospital,
London W.12

Treatment of Herpes Simplex with Co-trimoxazole

SIR,—I had deliberately kept my previous letters on this subject as short and non-technical as possible. However, I should be grateful for the opportunity to reply to the points made by Professor D. H. Watson and Dr. D. Haigh (1 February, p. 271).

The method of testing the effect of trimethoprim on herpes simplex virus (H.S.V.) used in the microbiology department of Raigmore Hospital was as follows: human amnion cells were inoculated with H.S.V. and trimethoprim was added to three specimens in concentrations of 2000, 1000, and 500 $\mu\text{g}/\text{ml}$ respectively. The highest concentration was found to be toxic to the cells; at the lower concentrations there was considerable reduction of cytopathic effect. As I pointed out (17 August 1974, p. 473) these levels are higher than the serum levels of trimethoprim that have proved therapeutically effective, but there is some evidence to suggest that levels of trimethoprim are

higher in tissue than in serum when both are estimated simultaneously,¹ and particularly with virus infections the tissue level seems likely to be more relevant. It has also been pointed out by Bushby² that in investigating the effect of various drugs on H.S.V. in vitro the inoculum must be small and care must be taken that the medium does not contain significant quantities of end products of folate metabolism.

Over the past 11 years or so a wide variety of drugs have been reported as effective against H.S.V., either clinically or experimentally. These have ranged from antihistamines^{3,4} to antimetabolic substances,⁵ but most interest has centred on cytarabine and idoxuridine, both being thought to work by interference with viral DNA synthesis.⁶ In particular, Delamore and Prusoff⁷ found that idoxuridine reduces the incorporation of ³H-thymidine into DNA-thymidine, but they noted that the specific metabolic site primarily affected in any given tissue is characteristic for that tissue. Hall *et al.*⁸ pointed out that viruses may induce new enzymes such as kinases and polymerases in infected cells, and Klempner *et al.*⁹ had already reported the finding of a virus-specific thymidine kinase in H.S.V.-infected cells. I had thought that I had already made it clear (4 January, p. 41) that the mode of action of co-trimoxazole against H.S.V. is as yet undetermined but that the similarity of the proportion of responders to that of subjects whose activated lymphocytes show inhibition by co-trimoxazole of their uptake of labelled thymidine¹⁰ leads me to suspect that thymidine metabolism in the host may be a relevant factor. The report by Hall *et al.*⁸ also stressed the probable importance of cell-mediated immunity in varicella infections, and in view of the close relationship between varicella-zoster virus and H.S.V. and the well-known finding that raised serum titres of H.S.V. antibody do not seem to confer any very noticeable protection against recurrent H.S.V. lesions it would seem logical to study the host cell at least as much as the virus.—I am, etc.,

PAULA H. GOSLING

Craig Phadrig Hospital,
Inverness

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Neonatal Hyperthyroidism and Long-acting Thyroid Stimulator Protector

SIR,—We read with interest the suggestion of Dr. J. Nutt and her colleagues (21 December, p. 695) that the case of L.A.T.S.-negative neonatal hyperthyroidism reported by Thomson and Riley¹ may have been due to long-acting thyroid stimulator protector (L.A.T.S.P.).

Serum was taken in November 1974 from the mother whose case was reported by Thomson and Riley.¹ Since the previous re-

port the patient's clinical state and therapy had remained essentially unchanged. This serum was in fact found to contain readily detectable L.A.T.S.P.,² whereas L.A.T.S. was not detectable. The results were as follows:

Sample	L.A.T.S. Response in Mouse Bioassay (% initial blood ¹³¹ I at 16h, mean $\pm$ S.E.M. (n))
Control for L.A.T.S. (control buffer, 1 ml)	89 $\pm$ 14 (3)
Test for L.A.T.S. (patient's serum 1 ml)	88 $\pm$ 9 (3)
Control for L.A.T.S.P. (human thyroid extract (H.T.E.) plus standard L.A.T.S.)	120 $\pm$ 4 (5)
Test for L.A.T.S.P. (patients' serum 1 ml plus H.T.E. plus standard L.A.T.S.)	383 $\pm$ 73 (3)
Standard L.A.T.S.	886 $\pm$ 104 (5)

*Student's *t* test.

Thyroid-stimulating activity in the mother was also detectable in the radioreceptor assay for thyroid-stimulating immunoglobulins:³

Sample	¹²⁵ I-Thyroid-stimulating Hormone Bound to Human Thyroid Membranes (%)
Patient's immunoglobulins (4 mg)	17.0
Normal immunoglobulins (4 mg)	20.9

Though almost 10 years have passed since the birth of the affected infant, we believe that this case provides evidence additional to that already reported^{4,5} for a causal role of L.A.T.S.P. in neonatal thyrotoxicosis. The receptor assay data confirmed the presence of human thyroid-stimulating activity in this serum.—We are, etc.,

J. A. THOMSON

University Department of Medicine,
Royal Infirmary,
Glasgow

S. M. DIRMİKIS
D. S. MUNRO

Section of Medicine,
Academic Division of Medicine,
University of Sheffield

B. R. SMITH
R. HALL
E. D. MUKHTAR

Endocrine Unit,
Departments of Medicine and Clinical Biochemistry,
University of Newcastle upon Tyne

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Tranquillizers Causing Aggression

SIR,—Your recent leading article (18 January, p. 113) referring to the possibility of benzodiazepine-induced hostility has prompted me to report a further example of this phenomenon, first reported in a patient in 1960.¹

The patient was a 35-year-old married woman who had been subject to idiopathic epilepsy since her early teens. She developed depression in the puerperium at the age of 32 and had been taking various psychotropic drugs in addition to her usual anticonvulsants. For some months she had been taking diazepam 5 mg three times a day, but often abused the drug by increasing the dose. She suddenly developed aggressive behaviour, attacking her husband and smashing some windows at home