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 14% operation mortality giving us the same three deaths 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


Reactions to Practolol

Sir,—In view of the recent reports of reactions to practolol, possibly on an autoimmune 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 myxœdema was admitted with angina. She had been treated for two years with practolol, bendroflumazide, slow-release potassium, digoxin, glycercyl 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 4 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, g-glutamyl transpeptidase, and bilirubin levels rose during the acute attack and are now normal.—We are, etc.,

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M. B. ABLETT

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Hamersmith 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 mg/ml respectively. The highest concentration was found to be toxic to the cells; at the lower concentrations there was a 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, and particularly with virus infections the tissue levels seem likely to be more relevant. It has also been pointed out by Bushby that in investigating the effect of various drugs on H.S.V. in vitro the virus inoculum 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 anti-histamines1 to antitubiotic substances,2 but most interest has centred on cytarabine and idoxuridine, both being thought to work by interference with viral DNA synthesis.3 In particular, Delamore and Prusoff4 have pointed out that idoxuridine reduces the incorporation of "H-thymidine into H.S.V.-DNA thymidine, but they noted that the specific metabolic site primarily affected in any given tissue is characteristic for that tissue. Hall et al5 pointed out that in the method 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 thymidine6 leads me to suspect that thymidine metabolism in the host may be a relevant factor. The report by Hall et al also stressed the 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.,

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Inverness

1 Drugs, 1971, 1, 9.

Neonatal Hyperthyroidism and Long-acting Thyroid Stimulator Protector

Sir,—We read with interest the suggestion of Dr. J. Nett and her colleagues (21 December, p. 695) that the case of L.A.T.S.P.-negative neonatal hyperthyroidism reported by Thomson and Riley7 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. Since the previous report 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., whereas L.A.T.S.W. was not detectable. The results were as follows:

<table>
<thead>
<tr>
<th>Sample</th>
<th>L.A.T.S. Response in Mouse Bioassay (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control for L.A.T.S. (patient's serum)</td>
<td>89 ± 14 (3)</td>
</tr>
<tr>
<td>Control for L.A.T.S. (human thyroid extract, H.T.E.)</td>
<td>88 ± 9 (3)</td>
</tr>
<tr>
<td>Test for L.A.T.S. (patient's serum)</td>
<td>120 ± 4 (5)</td>
</tr>
</tbody>
</table>

Patient's immunoglobulins (4 mg) Normal immunoglobulins (4 mg)

17.0 20.9

Thus although 10 years have passed since the birth of the affected infant, we believe that this case provides evidence additional to that already reported8,9 for a causal role of L.A.T.S.P. in neonatal thyrotoxicosis. The recurrence of the assay data confirmed the presence of human thyroid-stimulating activity in this serum.—We are, etc.,

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Tranquilizers 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.

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 pregnancy at the age of 32 and had been taking various psychotropic drugs in addition to her usual anticonvulsant. For some months she had been taking diazepam 5 mg three times a day, but often abused the drug by increasing the dose. She developed delusional aggressive behaviour, attacking her husband and smashing some windows at home.