complication which I find fairly frequently—namely, pain in the right subcostal area. I feel certain that it is a manifestation of change in the biliary system, but it is not a colic, the pain being dull and steady with tenderness in the same area. One patient had an area of paraesthesia in addition. It tends to continue intermittently throughout the prenatal course and disappears after delivery. To date I have found no good explanation for it, or method of relieving it, other than by using analgesics.—I am, etc.,

St. Joseph's Hospital,
Toronto, Ontario,
Canada.

J. L. FRASER.

REFERENCE

- ¹ Goodman, L. S., and Gilman, A. (editors), *The Pharmacological Basis of Therapeutics*, 1955, 2nd ed., p. 1194. Macmillan, New York.

Angor Animi

SIR,—A sense of impending dissolution—angor animi, is occasionally encountered in angina pectoris.¹ The dangers of direct interrogation of the patient about this symptom are vividly illustrated by the following case.

Some 10 years ago, when I was the admitting house-physician at a London teaching hospital, I was called to examine a man aged about 60 with a history of effort angina which had increased progressively during the preceding few weeks. He was sitting up in bed chain-smoking and appeared extremely tense. I inquired about the character and distribution of the pain and its relationship to exertion, and his replies were lucid and gave a classical picture of angina pectoris. I then inadvertently asked him whether he ever felt he was going to die during one of the attacks. He did not reply to this question but his attitude immediately changed. He seemed to become increasingly distressed and looked at me with fixed staring eyes. He died about one minute later while I was auscultating his heart. I do not remember the necropsy findings, but I imagine that the cause of death was coronary thrombosis, which may well have been precipitated by fright.

As a result of this alarming and unforgettable experience I have always refrained from asking patients with angina about this symptom.—I am, etc.,

Shelton Hospital,
Shrewsbury, Shropshire.

J. C. BARKER.

REFERENCE

- ¹ Price, F. W., *A Textbook of the Practice of Medicine*, 1950, 8th ed., p. 1059. Oxford Medical Publications.

Dequalinium and Balanitis

SIR,—Three colleagues have reported to one of us their suspicions that an association may exist between a form of ulcerating balanitis¹ and the use of dequalinium products.

There does indeed appear to be appreciable circumstantial evidence of a relationship between the use of these preparations (marketed as Dequadin or Dequalone P) and the occasional development of an unusual type of necrotic lesion. This happens only very rarely, but seems to do so especially in the treatment of balanitis.

Urgent steps are being taken to test the validity of the evidence and to explain the mechanism involved. But we feel meanwhile

that these preparations should not be used in the treatment of balanitis or under circumstances where the skin is occluded.

We would like to acknowledge the acumen of Drs. R. E. Church, J. G. Holmes, and R. P. Warin in recognizing this possibility and bringing it to our notice.—We are etc.,

Northampton.

Allen and Hanburys,
Ware, Hertfordshire.

Amersham.

R. B. COLES.

W. T. SIMPSON.

D. S. WILKINSON.

REFERENCE

- ¹ Wilkinson, D. S., *Brit. J. Derm.*, 1963, 75, 16.

Allergy to Tremonil

SIR,—The enclosed account of drug sensitivity may be of interest.

A spinster aged 68, suffering from cerebellar ataxia, came under my care in March 1963. At that time her blood-pressure was 210/120 and there was marked tremor and ataxia. She was given Aldomet (methyldopa), 250 mg. at night, and 10 mg. of Librium (chloridiazepoxide hydrochloride) t.i.d. Five days later, as there was not much change in her condition, the Aldomet was increased to 250 mg. night and morning. On 22 March 1963 her blood-pressure had fallen to 160/105 and the Aldomet was reduced to 250 mg. at night.

On 27 March she was seen by a neurologist who recommended starting Tremonil (methixene hydrochloride), half a tablet (2.5 mg.) three times a day. There was considerable improvement in her tremor and ataxia, and by 20 May she was taking one tablet (5 mg.) of Tremonil night and morning.

I was called suddenly to see her on 12 June 1963. Her face was swollen and there was oedema of her eyelids. She told me that three days previously she had sat in the sun for two to three hours and the following day she developed diarrhoea and vomiting and her face became swollen. At first I thought this was a reaction to sunlight, but by 14 June she had become extremely ill with a temperature of 101° F. (38.3° C.), blood-pressure 150/75, and there was a rash covering almost the whole of her body; at the same time she had a dry cough and there was bronchial breathing over the left upper zone both back and front. The urine contained a considerable quantity of albumin

and she told me she had been passing green stools and had vomited some black fluid. The Aldomet and Tremonil were stopped and she was put on Terramycin (oxytetracycline), 250 mg. six-hourly. The following day she was much improved, her temperature was normal, and the vomiting and diarrhoea had stopped.

On 17 June her urine was free from albumin and her lungs were clear. This was followed by a widespread desquamation of the skin and her tongue became extremely sore. On 28 June she was restarted on Tremonil, one tablet in the morning, but this was stopped on 9 July. On 16 August 1963, as her tremor and ataxia were very marked, Tremonil was again started, one tablet at night. At that time there was a small patch of eczema on her left second finger. A week later she was restarted on Aldomet, 250 mg. at night, and the following week her lips became swollen. Both Tremonil and Aldomet were stopped and the swelling subsided. Early in October the patient started taking an occasional tablet of Tremonil as she found this helped her tremor so much. In November 1963 she was taken off Tremonil and given Disipal (orphenadrine hydrochloride) tablets, but she felt that these did not help her tremor.

In view of her apparent sensitivity to Tremonil and/or Aldomet a new régime was started—namely Tremonil—one tablet at night for a fortnight and then the Tremonil was discontinued and Aldomet, one tablet (250 mg.) at night for a fortnight, was given. This arrangement seemed to suit her very well until 15 May 1964, when I saw her. At that time she had not taken Aldomet for between four and six weeks but had been taking Tremonil. There was an allergic rash on the dorsa of the fingers of both hands, the Tremonil was stopped, and the rash subsided. She had been off Tremonil since that date, and when seen last, one week ago, commented on the fact that since she had had this longer period off Tremonil her skin had improved considerably, and there seemed, on inspection, to be little doubt of the truth of her statement; the skin was much more supple and less dry than it had been previously.

I have reported this case to the Dunlop Committee and also to the manufacturers, Messrs. A. Wander Ltd. The latter told me that following my report they had received one other report of an allergic reaction apparently to Tremonil.—I am, etc.,

Pennington, Hants.

M. B. CARSON.

Oral Contraceptives and Liver Damage

SIR,—In their paper Drs. A. Eisalo and others (15 August, p. 426) reported their preliminary observations on hepatic impairment during the intake of Lyndiol. The oestrogen component given alone was hepatotoxic, while the progestogen component was without such an effect. We recently gave to five post-menopausal patients another contraceptive pill, Anovlar (Schering, Berlin, one pill containing 4 mg. of norethisterone acetate and 0.05 mg. of ethinyloestradiol). The progestogen component is a 19-nortestosterone

derivative other than that in Lyndiol, and the oestrogen component also is somewhat different. One pill daily was given to each patient.

The weekly S.G.O.T. values are presented in the Table. In every case the serum transaminase values were clearly elevated after one week's intake. In two patients who were kept in hospital after the treatment the S.G.O.T. values decreased when the drug intake was discontinued. Bromsulphthalein retention increased to pathologic levels

Biochemical Data on Subjects Taking Anovlar

Case No.	Age (Years)	Day and Results of S.G.O.T. Determinations						Observations on 14th Day		
		0	7	14	21	28	42*	B.S.P. Retentions (%)	Serum Bilirubin (mg. %)	Alk. Phosphatase (Units)
1	76	33	218	340	380	610	61	27	0.47	10.4
2	73	36	60	61	56	52	53	20	0.20	4.7
3	62	59	89	83	240			38	1.70	14.0
4	68	28	260	320	180			26	2.05	12.2
5	80	50	105	270				28	0.95	13.9

* Fourteen days after discontinuance of the drug. Note: B.S.P. retention in % of given dose (2 mg./kg.) after 45 min. (normal less than 8%). Alkaline phosphatase in King-Armstrong units (normal 5–11).

within two weeks in all patients. The alkaline phosphatase was slightly elevated in three cases, and the serum bilirubin pathologically high in two cases. Accordingly, the liver-function tests revealed a pattern of hepatic impairment fully similar to that observed by Eisalo *et al.*

Our series is small, but the hepatic injury occurred in every case during a very short observation period. It leaves no doubt about the hepatotoxicity of this contraceptive pill also. It is noteworthy that the daily dose of both progestogen and oestrogen in this series was clearly smaller than that used by Eisalo *et al.* We consider that a study of the hepatotoxic effect of even smaller amounts of norethisterone and ethinyloestradiol, and in a series of young women too, is indicated.—We are, etc.,

I. P. PALVA.

O. O. MUSTALA.

Second Department of Medicine,
University of Helsinki,
Unionink 38,
Helsinki, Finland.

Ruptured Uterus after Buccal Oxytocin

SIR,—Recently the use of oxytocin buccal tablets (trade name Pitocin Buccal) has been introduced in this hospital in some cases where we formerly used an intravenous infusion of Syntocinon (oxytocin). I would like to report a case of ruptured uterus which occurred after using this method of inducing uterine contractions.

Mrs. G., gravida four, aged 38, was admitted with a history of 31 weeks' amenorrhoea and a diagnosis of intrauterine death

at 24 weeks. It was decided to induce labour with stilboestrol and buccal Pitocin. She was given the tablets as recommended by the manufacturers—that is, tabs. $\frac{1}{2}$, $\frac{1}{2}$, 1, 1, 2, 2, 3, 3, 3, and so on, at half-hourly intervals until a satisfactory response was obtained, without exceeding 4,400 units. On the first day the course was abandoned after a total dose of 2,000 units because of a sudden rise in blood-pressure. In view of this a modified

course was given on the second day—tabs. $\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$, 1, 1, 1, 1, $1\frac{1}{2}$, $1\frac{1}{2}$, $1\frac{1}{2}$, 2, 2, 2, 2. In this way she received a total dose of 4,000 units in eight hours, when her contractions were of fair strength and quite regular.

Two hours after the course had finished her contractions were strong and very painful. On vaginal examination the presenting part was felt encircled by a rigid cervix. Morphine, gr. $\frac{1}{4}$ (16 mg.), was prescribed. During the next three hours her contractions continued almost painlessly, and during this time her blood-pressure slowly dropped from 130/80 to 80/60 mm. Hg. She appeared shocked and was found to be tender in the left iliac fossa with the uterus pushed over towards the right side. Six hours after stopping the buccal Pitocin she delivered, with some assistance, a macerated foetus of 26 weeks. Immediately afterwards it was apparent that there was a tender mass in the left iliac fossa and her condition suddenly deteriorated. Before laparotomy could be carried out she had to be transfused with three pints (1.7 l.) of blood and given an intravenous hydrocortisone infusion. At laparotomy a large haematoma was found in the left broad ligament; subtotal hysterectomy was then performed. The rupture extended along the lateral border of the uterine lower segment for $1\frac{1}{2}$ in. (3.8 cm.) (see Photos). Her post-operative recovery has been uneventful.

Since this accident we have read some of the previous reports concerning the use of this drug and realize that the schedule issued by the manufacturers suggests very high dosages. From our clinical observations there appears to be a marked cumulative effect when the number of tablets in the buccal space exceeds $1\frac{1}{2}$ tablets.—I am, etc.,

British Hospital for Mothers and Babies,
Woolwich S.E.18. P. M. LENEY.

Ulcerative Colitis in the African

SIR,—Following the report by Dr. J. R. Billingham (11 July, p. 117) of three cases of ulcerative colitis in the African may I record four other cases encountered in Africans in Durban in the past three years?

The first patient is a female teacher aged 27 years who had had dysentery for a year. She had attended other hospitals previously where anti-amoebic treatment failed to relieve her symptoms. She was emaciated and pale with a haemoglobin of 8.8 g. per 100 ml. Microscopic examination of the stools on numerous occasions revealed blood and mucus but no *Entamoeba histolytica*, and at sigmoidoscopy no amoebic ulcers were seen but the mucosa was observed to be friable and hyperaemic. There was no response to anti-amoebic treatment but she responded to steroids, blood transfusions, and salicylazosulphapyridine/sulphasalazine (Salazopyrin). Barium enema examination revealed loss of haustration of the descending and sigmoid colon and fuzziness of the contour of the ascending colon, caecum, and transverse colon, which appeared irregular. A repeat barium enema six months later showed no change. The remaining three patients, two females and a male, presented similar symptoms and signs and the duration in one was 14 years. None of the patients had any evidence of amoebic colitis.—I am, etc.,

Department of Medicine, V. K. G. PILLAY.
University of Natal,
and King Edward VIII Hospital,
Durban.

T.A.B. Reactions

SIR,—As far as systemic reactions to T.A.B. vaccination are concerned I agree with Dr. L. R. S. MacFarlane (15 August, p. 445) that the intradermal vaccine is preferable to the subcutaneous vaccine. Nevertheless, the severity of local reactions cannot in my opinion be regarded as negligible, especially if such a vaccine is recommended for use generally among civilians intending to travel abroad.

It was stated in a leading article (4 July, p. 3): "About 75% of people develop fever and malaise for 12–24 hours after inoculation by the usual subcutaneous route, but this can often be prevented by giving the injection intradermally (as one-fifth of the normal dose

of vaccine); occasionally the skin at the site of the injection may become tender." (My italics).

Intradermal vaccine of the same kind as that used in the British Army was recently given to 54 members of the staff of the Central Public Health Laboratory. It was injected intradermally in a dose of 0.1 ml. into the lateral aspect of the upper arm behind the posterior border of the distal portion of the deltoid muscle. A local reaction consisting of an area of erythema, oedema, induration, and tenderness about 3 in. (7.6 cm.) in diameter occurred in all persons. (See photograph taken 18 hours after intradermal inoculation).

It is not my intention to detract from the merit of intradermal T.A.B. vaccine, but to draw attention to the degree of local reaction which can occur.—I am, etc.,

A. J. ZUCKERMAN.

Diagnostic Reference Laboratory,
Central Public Health Laboratory,
London N.W.9.

Amalgamation of Armed Forces Medical Services

SIR,—The facile view of Dr. A. G. D. Whyte (5 September, p. 634) that "It will be a better day for all concerned when the obvious combined medical service for the armed Forces of the Crown comes along" should not be allowed to pass unchallenged.

The idea has been explored in detail by Government-sponsored inquiries in 1923 (Warren Fisher), 1946 (Nathan), 1956 (Waverley), and 1959 (Parliamentary Esti-