which classes of hyperlipoproteinaemia are best treated with a combination or with clofibrate alone. It is, however, quite clear that its greatest potential use is for the treatment of the type II pattern, which is, in general, affected little by clofibrate alone and only moderately by cholestyramine.

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MEDICAL MEMORANDA

Ischaemic Colitis and the Contraceptive Pill

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Ischaemic colitis is a well-defined clinical, radiological, and pathological entity (Marston *et al.*, 1966). It occurs most commonly in elderly patients with arteriosclerosis. Most younger patients have had associated conditions which predispose to embolism, venous thrombosis, or vasculitis, such as cardiac disease, diabetes mellitus, or rheumatoid arthritis (Lea Thomas, 1968).

We report a typical attack of ischaemic colitis occurring in a woman taking the contraceptive pill and discuss the possible causative relationship.

Case Report

A married woman aged 39 was admitted to hospital because of sudden severe colicky abdominal pain below the left costal margin associated with bloody diarrhoea. Her bowel habit had previously been normal apart from occasional blood loss due to haemorrhoids. She smoked 10-15 cigarettes a day. She had been taking Ovulen (ethynodiol diacetate 1 mg, mestranol 0·1 mg) cyclically as a contraceptive for two years. Two weeks before admission this had been changed to Ovulen 50 (ethynodiol diacetate 1 mg, ethinyloestradiol 0·05 mg).

On examination she was found to be moderately overweight and not seriously ill. Her temperature reached 38°C intermittently over the first few days. The left side of the abdomen was tender but there was no palpable mass or sign of peritonitis. Rectal examination and sigmoidoscopy showed internal haemorrhoids, normal rectal mucosa, and bleeding from above the rectosigmoid junction. There were no signs of peripheral vascular disease or arthritis. The cardiac rhythm was regular and the blood pressure 120/70 mm Hg.

On admission the haemoglobin was 14·0 g/100 ml; W.B.C. 12,400/mm³ (91% neutrophils); E.S.R. 12 mm/hr (Westergren); platelets were 210,000/mm³; and serum protein electrophoresis was normal. There was no glycosuria and no pathogens were isolated from the stools or urine. Plain *x*-ray films of the abdomen showed absence of gas in the splenic flexture and descending colon.

Barium-enema examination five days after the onset of symptoms showed a narrowed segment from the splenic flexure to about halfway down the descending colon, merging gradually into normal colon at either end. The margin of the segment was irregular and showed evidence of "thumb-printing" (Fig. 1 A). An abdominal aortogram performed by flood aortic injection in the prone position showed normal origins of the coeliac axis and superior and inferior mesenteric arteries. No abnormality of their distal branches or of the marginal artery was seen.

The abdominal pain, tenderness, and fever settled within three days without specific treatment. The diarrhoea ceased after the first day and there was no further bleeding. Oral contraceptives were discontinued and she left hospital after 11 days.

A repeat barium-enema examination a month after the first showed that the segment had considerably widened; the thumb-printing had disappeared but there was some evidence of sacculation (Fig. 1B). She had no recurrence of symptoms, and a third enema eight months after the first showed that the colon had returned to normal (Fig. 1 C).

Comment

The clinical course and radiological features in this patient were typical of ischaemic colitis. She had a sudden onset of left-

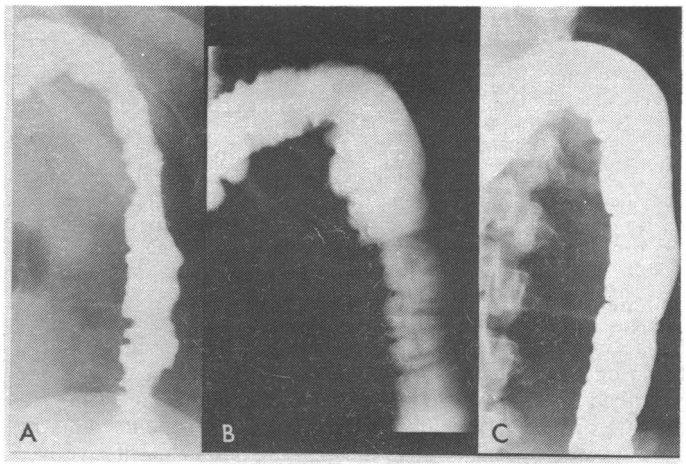

FIG. 1—A, First barium-enema film showing narrowing and thumb-printing of the splenic flexture and descending colon. B, One month later. The segment has widened and sacculation has developed distal to the splenic flexture. C, Eight months later, normal.

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sided abdominal pain followed by bloody diarrhoea which rapidly improved without specific treatment. The barium-enema examination showed changes at the typical site which progressed from narrowing with marginal thumb-printing, through sacculation, to complete normality (Boley *et al.*, 1963; Marston *et al.*, 1966; Lea Thomas, 1968; Williams *et al.*, 1969). The only unusual feature was the patient's age and sex. The condition usually occurs in the age group at risk from degenerative vascular disease, more common in men (Morson, 1968). In a series of 36 patients with a mean age of 62 (range 42-82) reported by Lea Thomas (1968) the younger patients were mainly women with cardiac or rheumatoid disease.

Though the morbidity is that of acute ischaemia (Marston *et al.*, 1966, 1969; Morson, 1968) and large and small arterial changes may sometimes be found, aortography usually shows nothing abnormal, possibly because the smaller arteries and veins cannot be seen by this technique (Lea Thomas, 1968).

In view of this patient's age and sex and the absence of other precipitating factors it is reasonable to discuss her use of the contraceptive pill. An increased risk of pulmonary embolism, deep-vein thrombosis, and cerebral and coronary thrombosis has been established in women taking oral contraceptives in the United Kingdom (Inman *et al.*, 1970), especially those containing larger amounts of oestrogens. Gangrene of the small bowel, superior mesenteric artery thrombosis (Brennan *et al.*, 1968), and also mesenteric venous thrombosis (Reed and Coon, 1963); Civetta and Kolodny, 1970) have been described.

Kilpatrick *et al.* (1968) discussed the cases of two patients aged 29 and 32 taking oral contraceptives who showed radiological evidence of transient ischaemic colitis. These patients together with the present case suggest an aetiological relationship. We feel that ischaemic colitis should be considered in all young women who present with acute abdominal pain and blood-stained diarrhoea who are taking a contraceptive pill.

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Bullous Lesions in Nitrazepam Overdosage

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The appearance of bullae on the skin in unconscious states has been well attested. Much of the work has referred to cases of barbiturate poisoning. In the case described below there was strong evidence to suggest that the patient had taken nitrazepam (Mogadon) and none to suggest that she had taken barbiturates.

Case Report

A woman aged 24 was admitted to hospital deeply unconscious There were tense bullae, some haemorrhagic and some on a reddened base, affecting the left side of the face, left hand and wrist, and left breast. There was no evidence on searching, checking with doctors who had seen her, or, later, questioning the patient that she had taken barbiturates, there was firm evidence that nitrazepam had been prescribed, and the patient stated that she had taken 100 tablets of this drug.

She recovered uneventfully after having been unconscious for about 36 hours, and the bullae healed to leave considerable scarring. There were psychiatric problems and she did not attend for follow-up. It was learnt a few months later from her general practitioner that she had scarring involving the carpometacarpal and metacarpophalangeal joints of her thumb and that she was having physiotherapy elsewhere, plastic surgery also having been considered.

Comment

Bullae in comatose patients have been noted for many years. Beveridge and Lawson (1965) reviewed the literature, described bullae in 19 out of 290 patients suffering from barbiturate overdose, and found no bullae in 69 patients suffering from overdosage of other drugs—phenothiazine derivatives and non-barbiturate hypnotics. Beveridge (1970) reported that histologically necrosis of the epidermis, involving the sweat glands, was seen in some affected patients, prompting the idea that barbiturate might be excreted by these glands.

Gröschel *et al.* (1970) reported a case of barbiturate overdosage with bullae in which the blister fluid contained barbiturate. Mandy and Ackerman (1970), pointing out that bullae in carbon monoxide poisoning were described by Schmidt in 1865, surveyed reports of coma of other origin in which bullae had been described, including that produced by methadone, hydrocodone bitartrate, meprobamate, imipramine, and glutethimide. These authors themselves found bullae in 4% of 501 cases of barbiturate poisoning and in 40% of 300 patients dying from this cause. They stressed that bullae are not found in the absence of unconsciousness and suggested that trauma and hypoxia are aetiological factors.

It seems therefore that the presence of bullae in a comatose patient by no means indicates that barbiturates are the cause of the coma. In the collection of hypnotics which have been incriminated nitrazepam seems not to be recorded, and it is not chemically related to those which have been noted. That cases have occurred before, however, seems clear from the experience of R. Goulding (personal communication, 1970) at the Poisons Reference Service of Guy's Hospital.

Finally, as Freeman and Raza (1965) point out, bullae apparently identical can be seen in patients with coma of neurological origin in which there is no question of the ingestion of hypnotics; and they record two such cases.

It may be concluded that the bullae represent a reaction to pressure and hypoxia in the skin of the unconscious patient. Barbiturates have often been incriminated because they are a frequent cause of coma.

I should like to thank Dr. A. L. Jacobs for permission to publish details of this patient who was admitted under his care, and Dr. C. W. L. Smith for supplying details of her subsequent course,

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