starting treatment with diltiazem the drug should be stopped and both renal and hepatic function monitored.

We are grateful to the coroner and to Professor J M Cameron for performing the necropsy. The medical artists of the London Hospital Medical College and Mr John Golden prepared the figure.

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Role of maternal age in assessment of risk of abortion after prenatal diagnosis during first trimester

In a consecutive series of 546 pregnancies after chorionic villi sampling for prenatal diagnosis during the first trimester we studied certain variables that might influence the risk of abortion in continuing normal pregnancies, including quantity of collected tissue, number of catheter insertions, and maternal age.

Patients, methods, and results

A series of 546 consecutive normal pregnancies at risk of genetic disease was monitored, and prenatal diagnosis was attempted during the first trimester. Chorionic tissue was collected by the transcervical route[1] by means of Portex, and later Angiomed, catheters.[2] Sampling was performed during gestational weeks 9-11, with a real time sector scanner (Diasonics DFR 1, carrier frequency 5 MHz), when culture of the cervical smear yielded negative results. The catheter was inserted no more than three times. Results of karyotyping and metabolic studies were available within two days, and those of deoxyribonucleic acid studies within two weeks. Patients were monitored up until 28 weeks' gestation. Statistical analysis was by Fisher's one tailed test. An abnormal fetus was diagnosed in 42 pregnancies and the prenatal diagnoses were confirmed by cytogenetic examination after elective abortion. No correlation was found between the quantity of collected chorionic tissue and the abortion rate.

In nearly half the pregnancies the catheter had to be inserted two or three times to collect enough tissue for multiple analyses. The rise in abortion rate with the increasing number of insertions was not significant.

Relation between number of catheter insertions for chorionic villi sampling and abortion rate in 276 mothers aged 36 years or over and 228 younger mothers. Values are numbers (percentages) of abortions

	No of catheter insertions		
	1	2	3
Mothers aged <36 years:			
10-16 weeks' gestation	2 (1·7)	1(1·3)	1 (2·7)
16-28 weeks' gestation	1 (0·9)	1 (1·4)	
Mothers aged 36 years or over:			
10-16 weeks' gestation	5 (3·0)	4 (5·2)	4 (12·5)
16-28 weeks' gestation	4 (2·4)	3 (4·1)	

A total of 276 pregnancies (55%) were in women aged 36 years and over. The abortion rate in this group was 7·2% (20/276) compared with 2·6% in women under the age of 36 (6/228) ($p<0·01$). When these figures were related to the number of times the catheter was inserted, in those over 36 the abortion rate before 16 weeks' gestation rose from 3% after one insertion to 12·5% after three insertions ($p<0·05$). The rate in the group aged less than 36 years was equally distributed and remained below 3% (table).

Comment

The outcome of pregnancy is known to be worse in older mothers.[3] In the present study a significantly higher abortion rate after chorionic villi sampling was seen in mothers aged 36 and older. In this group the abortion rate was also related to the number of times the catheter was inserted. The observed rise in abortion rate with the increasing number of catheter insertions was mainly in pregnancies of less than 16 weeks' gestation.

After one catheter insertion the abortion rate was 3% up to 16 weeks' gestation and 2·4% between 16 and 28 weeks. This suggests that the risk after the minimum number of entries into the uterus is low compared with the overall abortion rates in pregnancies of comparable gestational age that are normal on ultrasound scanning; these are 4·5% in women aged 35-39 and as high as 13·6% in those aged 40 and over.[4]

In the group of younger mothers the number of catheter insertions did not influence the abortion rate, which was 1·7% before 16 weeks' gestation and only 0·9% between 16 and 28 weeks. After repeated catheter insertions the rate did not change significantly. The reported abortion risk in pregnancies of the same gestational age that are normal on ultrasound scanning was 2·1-2·5%.[4] The abortion risk after 16 weeks was comparable with the risk after amniocentesis for both younger and older mothers.[5]

We conclude that maternal age of 36 years or more adds another risk factor in continuing normal pregnancies after chorionic villi sampling, and causes a significant increase in the abortion rate, especially when repeated catheter insertions are necessary.

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Effect of diabetes on porphyric attacks

Acute intermittent porphyria is a not uncommon disorder of haem metabolism characterised by the accumulation of two haem precursors—namely, δ-aminolaevulinic acid and porphobilinogen. Two of the enzymes occurring in the synthesis of haem are affected in this type of porphyria[1]—namely, uroporphyrinogen-I-synthase, which is genetically deficient, and δ-aminolaevulinic acid synthetase (the first and rate limiting enzyme of the biosynthetic chain), which is secondarily induced. The occurrence of porphyric crises depends mainly on additional induction of this enzyme by several factors (starvation, infection, stress, and so on) or drugs[2] (barbiturates, anaesthetics, and so on). Glucose depresses the synthesis of δ-aminolaevulinic acid synthetase[3] and thus can minimise the accumulation of toxic haem precursors in acute porphyrias. Thus a high intake of glucose is recommended for preventing and treating porphyric attacks.

Case report

A 57 year old man who had had acute intermittent porphyria attended for a routine examination. Porphyria had been diagnosed when he was 31; before that he had had two operations because of severe attacks of abdominal pain. After diagnosis he had had several porphyric attacks (one or two a year), three of them being severe enough to require admission to hospital. Two of his daughters also showed signs of clinical porphyria.

During the past 10 years his porphyric attacks had completely stopped. Our routine examination showed type II diabetes mellitus; it was well controlled by

sugar restriction and metformin. Biochemical tests showed: serum glucose concentration 6·7-10 mmol/l, glycosylated haemoglobin 11·2%, urine δ-aminolaevulinic acid concentration 69·5 μmol/l (normal <38 μmol/l), urine porphobilinogen concentration 37·1 μmol/l (normal <13·2 μmol/l), and erythrocyte uroporphyrinogen-I-synthase activity 5·4 nmol/h.l (normal 10-32 nmol/h.l).

Comment

In patients who have acute intermittent porphyria porphyric attacks often tend to be less frequent and finally stop after the age of 40. The stopping of these attacks in our patient, however, was somewhat surprising, not only because his porphyria was aggressive but also because it stopped rather too abruptly. On the other hand, it is obvious that this period free of attacks coincided well with the latent and early clinical stages of diabetes. As a high intake of glucose or carbohydrate offers protection from porphyric attacks[1 4] it is not unreasonable to suggest that constant hyperglycaemia due to latent or overt diabetes can have a similar effect.

This assumption seems to agree with recent experimental findings in rats that have had diabetes induced by streptozotocin.[5] In these animals δ-aminolaevulinic acid synthetase activity showed a 36% decrease but was restored to normal values after treatment with insulin.

There are some sporadic reports of diabetes mellitus in patients who have acute intermittent porphyria, but we have found no mention of the course of the porphyria after the onset of diabetes.[4] Our patient will possibly have a lifelong remission from his porphyria if he is not overtreated for his diabetes. Thus we have avoided severely restricting his carbohydrate intake (monosaccharides and bisaccharides excluded), although he was overweight. He was given metformin as it does not produce hypoglycaemia and sulphonylureas are contraindicated in porphyria.[2]

Patients who have a long remission from porphyric attacks should be investigated to see if they have subclinical diabetes.

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Steroids, non-steroidal anti-inflammatory drugs, and serious septic complications of diverticular disease

Colonic diverticular disease may be present in as many as one third of people aged over 60.[1] Complications requiring surgery, however, occur in only a small proportion of those who have this condition, and the most serious complication—that of generalised peritonitis—is quite uncommon.[2] Because of this the factors that determine the development and severity of these complications are not well understood. A connection between corticosteroid treatment and severe septic complications of diverticular disease has been reported.[3] In addition, an increased risk of perforation of the small and large bowel, not necessarily related to diverticular disease, has been found in patients who were taking a variety of anti-inflammatory drugs.[4]

We present here evidence that supports an association between severe septic complications of diverticular disease and both corticosteroid and non-steroidal anti-inflammatory drug treatment.

Patients, methods, and results

Patients undergoing operative treatment for diverticular disease or its complications at Ipswich Hospital from 1972 to 1985 were identified from data from the Hospital Activity Analysis and operating theatre records. Patients who were not operated on and who died from complications of diverticular disease and underwent necropsy were also identified. For 192 patients (median age 67 years, range 25-88, 76 men) records were adequate for a retrospective analysis of drug history and operative and pathological findings.

When patients were divided into eight groups according to these findings there seemed to be an excess of patients who were taking corticosteroids or non-steroidal anti-inflammatory drugs among those who had the most serious complications (table). Logistic regression analysis was therefore used to compare patients who did and did not have extracolonic sepsis after allowance for any confounding effects of age and sex. The extension of sepsis outside the colon was strongly associated with both corticosteroids (relative risk=13·2, 95% confidence interval 1·81 to 96·5) and non-steroidal anti-inflammatory drugs (relative risk=4·85, 95% confidence interval 1·58 to 14·8).

Complications in patients treated for colonic diverticular disease. (Figures are numbers of patients)

Complication	Total	Treatment		
		Corticosteroids	Non-steroidal anti-inflammatory drugs	Both
No extracolonic sepsis:				
Diverticular disease only	16		2	
Inflammatory mass confined to colon	46		2	
Colonic adhesions but no extracolonic pus	15	1		
Extracolonic sepsis:				
Fistula	17	2	2	1
Extracolonic abscess	26	2	3	1
Purulent peritonitis	51	6	13	3
Faecal peritonitis	18	2	2	2
Septicaemia and portal pyaemia	3			1

There were 12 different indications for the corticosteroids and non-steroidal anti-inflammatory drugs taken by the patients who developed extracolonic sepsis, the most common being osteoarthritis (14 patients).

Comment

These findings support the previously reported association between corticosteroid treatment and severe septic complications of diverticular disease.[3] They also suggest an association between these complications and the use of non-steroidal anti-inflammatory drugs. This is consistent with the increased incidence of perforations of the small and large bowel previously reported in patients who were taking these drugs.[4] Such associations could have arisen because septic complications are related to an underlying condition for which steroids and non-steroidal anti-inflammatory drugs are prescribed. In this series, however, there were many different indications for treatment, and none could explain the association on its own. Another possibility is that the drugs impair the ability of the colon to limit or terminate inflammatory processes occurring within diverticula. Alternatively, or in addition, they may mask symptoms so that patients present with more advanced disease.

In view of the comparative rarity of serious complications of diverticular disease and the great benefit that steroid and non-steroidal anti-inflammatory drug treatment can give, it would be incorrect to withhold these drugs from an elderly person for fear of producing complicated diverticulitis. Caution, however, should probably be exercised when prescribing such drugs for patients who have a history of diverticulitis.

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