tee that the disease is still curable even when hospital attendance quickly follows the onset of symptoms.

Loin pain may sometimes be due to the associated hydro-nephrosis, but is often caused by extensive local infiltration of the paravertebral and vertebral tissues, which is synonymous with inoperability.

The presence or absence of haematuria has, in our experience, proved to be of little value in deducing either the size or the pathological picture of renal parenchymal tumours, but it is rare for a tumour of the renal pelvis to occur without bleeding.

The close relation between the cells of all three types of renal tumours and the blood vessels of their stroma increases the risk of distal dissemination. Occult metastases (Shackman and Harrison, 1948) may already be present at the time of operation, and there is a considerable risk of vascular dissemination as the result of handling the tumour at operation unless early ligation of the renal pedicle is practised. This is best achieved through an abdominal or thoraco-abdominal incision.

The prognosis in any individual patient depends not only on the histological grading of the primary tumour but also on the presence or absence of metastases. The former may be accurately assessed by the microscopist (Riches, Griffiths, and Thackray, 1951), but the latter is often proved only by time. Subsequent appearance of metastases after nephrectomy represents the progress of previously present but "hidden" tumour deposits.

All the surgeon can do is to extirpate, where possible, the primary tumour and the associated lymph nodes, and on occasion an apparently isolated distal metastasis. The radiotherapist may have something more to offer, but our experience in this direction, admittedly limited, has not been particularly encouraging.

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The Association of Children's Officers has prepared a memorandum, *Cruelty to Children*, in response to a request made by the Joint Committee of the B.M.A. and the Magistrates' Association. The memorandum sets forth the views of children's officers on the secondary effects of cruelty to children, its definition, types, causes, and incidence. Remedies for neglect and physical violence are not difficult to apply, but prevention of mental cruelty is a much wider problem, says the memorandum, and one on which a lead can be given only by the medical profession, for there is as yet little public awareness of emotional suffering. The legal remedies are outlined and the importance of stable family life as a factor in reducing cruelty is stressed. The economic aspect of prevention is also considered. It may cost up to £5 a week to maintain a child in a children's home, over £6 in an approved school, and as much as £8 in a residential nursery. Children should not be removed from home simply for failure to attend school; it is less expensive to send the school attendance officer to fetch them every day. They should not be removed simply because the home is dirty; it is less expensive to put in a family service unit. Neither should they be removed simply because the house is overcrowded or insanitary or because there is no house; it is less expensive to provide a house. Children should not be removed from their mother simply because she is widowed, unmarried, or deserted, and so has to go out to work; it is less expensive to pay an adequate National Assistance allowance to keep her at home with them. The memorandum is obtainable from the association at Bradninch Hall, Castle Street, Exeter, price 4d.

PEPTIC ULCER IN WOMEN

BY

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Many writers have claimed that the symptoms of peptic ulcer—and presumably its activity—are influenced by menstruation and by pregnancy. Thus Taussig (1908), Sutherland (1910), and Szenes (1924) have suggested that menstruation causes an exaggeration of the symptoms of ulcer, while Mussey (1927), Crohn (1927), Hurst and Stewart (1929), and many others have claimed that pregnancy commonly has a beneficial effect. There is some evidence also to suggest that the symptoms of ulcer may be influenced adversely by the onset of the menopause. The investigation reported below was designed to test the validity of these observations.

The evidence here presented was obtained by interviewing 400 women in whom peptic ulcer had been demonstrated either by radiology or at operation. The ulcer was duodenal in 330 cases, gastric in 70. The patients' ages ranged from 21 to 74 years. In most cases the symptoms were of more than five years' duration.

Method of Interview

In a disease which remits and relapses with such facility the manner of eliciting and correlating the evidence is obviously of importance. During the interviews every effort was made to eliminate the element of suggestion. Much of the information was volunteered; much was obtained by questioning, as indirect as possible; some had to be obtained by direct questioning. All of these women had already been interviewed at least once previously, and the standard case record of the peptic ulcer clinic had been completed, so that information was already available on such relevant points as year of birth, age of onset of symptoms, and age at which complications occurred. At interview for the present investigation these points were confirmed. Thereafter inquiry was made into the gynaecological and obstetric history—for example, age at menarche, age at which pregnancies occurred, age at menopause, etc. Finally the effect of those events on the ulcer history was correlated.

Often the patient volunteered some information. If not, the standard questions were asked, "Have you noticed any relationship between your ulcer and menstrual period/pregnancy/menopause? Was your ulcer made better or worse, or did it remain the same? Apart from paraphrasing these questions according to the patient's understanding of them, no further attempt was made to elaborate a correlation. According to the patient's answer, "better," "worse," or "no change noted," the results were assessed. If a relationship had been noticed inquiry was made into the time relationship and the quality and quantity of the worsening or improvement.

Menstruation

Of the 400 patients, 291 had had ulcer symptoms before the menopause. In this group 81 (28%) claimed to have noted some relationship between menstruation and the occurrence of ulcer symptoms. In all these cases the symptoms were worse for a few days or a week before the onset of menstruation. In eight the ill-effect persisted during the menstrual period. In none had the symptoms been noted to increase in the post-menstrual phase.

In interpreting these findings it must be remembered that the symptoms of quite unrelated diseases may be aggravated in the pre-menstrual phase—the result, perhaps, of psychic influences or of the general malaise which many women experience at that time. In those patients who had noted pre-menstrual increase of symptoms there was no evidence

to indicate whether the exacerbation was due to such causes or to factors directly related to the menstrual cycle, or even to the use of aspirin and similar analgesics. On the whole, however, it may be concluded from the present series that the effect of menstruation on ulcer symptoms is inconsiderable.

Pregnancy

In assessing the effect of this state on the symptoms of peptic ulcer it must be remembered that normal pregnancy in healthy women is commonly associated with symptoms not unlike those of peptic ulcer.

Nausea, vomiting, and heartburn are said to occur during the first few months of pregnancy in almost 40% of cases. Usually they disappear about the end of the third month, but they may persist until term. Occasionally more severe dyspepsia occurs, and its resemblance to ulcer is heightened by the relief afforded by antacids. Rarely, hyperemesis gravidarum may lead to confusion.

In attempting to decide whether such symptoms were attributable to the ulcer, attention was paid to their severity and to the patient's own view regarding their origin. With their previous experience of peptic ulcer, most of the patients with heartburn, nausea, and vomiting during the early months attributed the symptoms to pregnancy and regarded the ulcer as "cured." In cases with more severe pain, relieved by alkalis, the patients were unable to distinguish it from the previous ulcer dyspepsia.

Of the total of 400 women 118 had been pregnant (see Table). The total number of pregnancies was 344. Of these, 313 had occurred subsequent to the onset of the peptic ulcer. On the criteria laid down above, it is believed that

Effect of Pregnancy

Total no. of women	400
Women with pregnancies	118
Total no. of pregnancies	344
No. of pregnancies after onset of ulcer symptoms	313
Free from ulcer symptoms	140 (44.8%)
Improved	136 (43.4%)
Not improved	37 (11.8%)

pregnancy was associated with a remission of the ulcer symptoms in 276 cases (88.2%). More than half of these patients claimed to have been completely symptom-free during the whole pregnancy; the remainder had minor symptoms which they regarded as unconnected with ulcer. In the remaining 37 pregnancies (11.8%) symptoms persisted which were indistinguishable from those of ulcer. In some of these the symptoms were much worse than previously, and 14 of the patients were admitted to hospital for treatment of the indigestion. At least four of these were found to have albuminuria, and it is possible that the exacerbation was not entirely due to renewed activity of the ulcer. In no case did a complication of ulcer (haemorrhage or perforation) occur during pregnancy.

Thus it would appear that in almost 90% of ulcer patients symptoms are in abeyance during pregnancy. In some of the cases the ulcer had been inactive immediately before conception, and in them the remission persisted. In others the symptoms cleared up dramatically at an early stage of the pregnancy. In still others they improved gradually or became obscured by minor symptoms attributed to the pregnancy itself. Several patients averred that their successive pregnancies had been their only eupeptic respites and that they had enjoyed the pregnant state for the well-being it afforded.

The benefit derived from pregnancy is generally short-lived, as Fig. 1 shows. By the end of the third month after parturition symptoms had recurred in almost half the cases, and by the end of the sixth month in three-quarters. At the end of two years almost every patient had suffered a recurrence.

Menopause

The distribution curve of the ages of the 400 patients at the onset of ulcer symptoms is shown in Fig. 2. In Fig. 3 it is compared with a similar curve for male patients, based

upon figures derived from 1,393 cases from the peptic ulcer clinic. It will be seen that, while in both sexes there is a steep rise of incidence between the ages of 15 and 24 years, thereafter there is a difference, in that in females there is a deficit during the age period 25-40 years, followed by a

% RECURRENCE

FIG. 1.—Recurrence of ulcer symptoms after parturition.

NO. OF CASES

FIG. 2.—Age at onset of symptoms of peptic ulcer in 400 women.

% CASES

FIG. 3.—Age at onset of symptoms of peptic ulcer in males (1,393) and females (400).

secondary rise of incidence between 40 and 50. These features suggest a possible relation to the child-bearing period and the menopause.

In order to explore this possibility the time relationship between the onset of ulcer and the menopause has been noted in 204 of the women. In Fig. 4 these cases have been plotted in five-year groups according to whether the ulcer began to produce symptoms before or after, or about the time, of the menopause. Those cases in which ulcer symptoms developed in the five-year period which includes the year of the menopause and the two years before and after it are recorded at M. Others are included in the appropriate earlier or later five-year groups. It will be seen that there is a striking peak of incidence at or about the menopause.

The remaining 196 women have not yet attained the menopause. In order to produce a composite curve, comparable with Fig. 2, relating all 400 cases to the menopause, the onset of ulcer symptoms in this remaining group has

FIG. 4.—Relation of age at onset of symptoms to date of menopause in 204 women who have reached or passed the menopause.

FIG. 5.—Relation of age at onset of symptoms to actual or expected date of menopause.

been related to the expected age for that event. On the information available for the 204 cases the age of menopause varied between 37 and 56 years, with over 90% between 40 and 50 years; the average was 45 years, and this figure was treated as the expected age of menopause in the remaining 196 cases.

Working on this basis, Fig. 5 shows the time relation of the onset of ulcer symptoms to the actual or expected age of menopause in the whole series of 400 cases. It will be seen that it again emphasizes the two peaks of incidence in women, the former occurring in later adolescence and early adult life, the latter at about the time of the menopause.

FIG. 6.—Duodenal ulcer (330). Relation of age at onset of symptoms to actual or expected date of menopause.

FIG. 7.—Gastric ulcer (70). Relation of age at onset of symptoms to actual or expected date of menopause.

FIG. 8.—Relation of date of complications (haemorrhage or perforation) to actual or expected date of menopause (haemorrhage 95, perforation 33).

In this series of 400 there were 330 patients with duodenal ulcer and 70 with gastric ulcer. In Figs. 6 and 7 the two types have been treated separately in the manner described above for the series as a whole. It will be seen that the menopausal rise of incidence is not confined to one type, though, perhaps owing to paucity of numbers, the peak is less evident in the case of gastric ulcer.

In those women who had had ulcer symptoms before reaching the menopause inquiry was made concerning the progress of the symptoms at that time. There were 92 in this group and 41 (45%) of them either volunteered or agreed on indirect questioning that their symptoms had worsened at or about that time. This trend was confirmed by the fact that a large number of them were then constrained to attend hospital for the first time on account of ulcer symptoms.

The incidence of complications of ulcer gives added evidence of the harmful effect of the menopause on the activity of the lesion. Among the total series of 400 patients there was a history of 128 complications (95 haemorrhages and 33 perforations). Fig. 8 shows the time of occurrence of those complications in relation to the expected or actual time of the menopause. It will be seen that again there is a striking correlation, the number of complications occurring in the five-year period centred on the year of menopause being more than double that of any earlier or later period. Study of individual case records seems to give emphasis to the correlation, for several patients had more than one complication within a short time of the menopause, while one had two haematemeses and two perforations within the actual five-year period.

Discussion

Since peptic ulcer is prone to spontaneous remissions, great caution is necessary in attributing variations in symptoms to external events. However, the regularity with which remission of symptoms occurs in pregnancy and the frequency with which ulcers start, flare up, or undergo complications at or about the time of the menopause give us justification for concluding that those two states do influence the activity of the ulcer.

The manner in which they do so is uncertain, but two lines of speculation suggest themselves. (1) The effect of psychological disturbances on gastric function has been known for a long time, and has been demonstrated convincingly in recent years by many workers, notably Mittelman and Wolff (1942) and Wolf and Wolff (1943). It may well be that the remission of ulcer symptoms in pregnancy is related to the general feeling of well-being, success, and fulfilment characteristic of that state, while the mental stresses, irritability, and emotional imbalance of the menopause may account for the renewed ulcer activity at that time. (2) The mechanism may possibly be a hormonal one. It is well established that pregnancy is a period of increased hormonal activity with a marked increase in the gonadotrophic, luteal, and oestrogenic hormones, while the menopause is associated with a diminution in the sex hormones, and particularly the oestrogens.

Recent reviews of the literature by Sandweiss *et al.* (1939), Bralow *et al.* (1948), and Sandweiss (1951) make it clear that despite much research there is no clear proof of a relationship between the sex hormones and peptic ulcer. Certainly the use of these hormones in the treatment of ulcer has been disappointing, though it should be observed that they are present in pregnancy in much larger amount than can be given therapeutically.

Summary

The natural history of peptic ulcer in 400 women has been investigated with reference to menstruation, pregnancy, and the menopause.

Menstruation has an inconsiderable effect on ulcer symptoms.

Relief of symptoms occurred in nearly 90% of pregnancies. In most of them the remission occurred early

in pregnancy and persisted until term. Those patients who gained no relief had a higher proportion of abnormalities such as albuminuria and hyperemesis.

After parturition, recurrence of ulcer symptoms was common, especially during the first six months.

An unduly large proportion of ulcers start, flare up, or undergo complications at or about the time of the menopause.

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A CASE OF GRANULOMA INGUINALE IN SCOTLAND: RESPONSE TO AUREOMYCIN

BY

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Granuloma inguinale, first described by McLeod (1882) and later by Conyers and Daniels (1896), is often thought of as a tropical disease, but it has been found in almost every country and climatic zone. Donovan's non motile encapsulated cocco-bacillus, long regarded as the probable causal agent, has been confirmed in this role by inoculation experiments in negro volunteers (Greenblatt *et al.*, 1939; Dienst *et al.*, 1947). Anderson (1943) described a method of cultivating the organism in the yolk sac of developing chick embryos; Dunham and Rake (1948) and Dienst (1948) reported successful culture in an artificial medium consisting mainly of yolk obtained from both fertile and infertile eggs. A positive skin reaction in human cases of the disease has been demonstrated by Kornblith (1944), with triturated infected material as antigen, and by Dienst *et al.* (1947), with a yolk sac culture of Donovan's organisms.

Although similar to the response evoked by the Leishman-Donovan body and by *Histoplasma capsulatum* (Hutchison, 1952), the lesion in granuloma inguinale differs from these by the presence among its predominating plasma-cell and endothelial-cell masses of small polymorphonuclear micro-abscesses described by Allen (1948). Pund and Greenblatt (1937) showed that the organism has a characteristic morphological appearance in the tissues of the host, and the demonstration of these bodies is a further point in the differentiation of these lesions from leishmaniasis and histoplasmosis. An even closer similarity is seen to the lesions of rhinoscler-