ENDOMETRIOSIS

By R. M. FEROZE, M.D., F.R.C.S., M.R.C.O.G.

Obstetric and Gynaecological Surgeon, King's College Hospital; Surgeon, Chelsea Hospital for Women.

Endometriosis is disease in which tissue resembling more or less perfectly the endometrium is found in ectopic sites; these sites are usually confined to the pelvis, but extra-pelvic lesions are also encountered. The condition is common in women who are infertile or relatively infertile. It usually begins to cause symptoms around the age of thirty years, and the disease is then progressive in most cases until ovarian function ceases. In those women who have borne children, and they seldom have had more than one, the symptoms follow some nine to ten years after the last confinement. Meigs (1949) is of the opinion that self-imposed infertility is conducive to the development of endometriosis, but there is no doubt that the disease, once present, is itself a serious obstruction to conception. The nature of the condition remains somewhat of a mystery, for whilst it is capable of forming tumours of a kind, these do not behave like either true benign or malignant tumours and, unless stromatous endometriosis be included, they never directly cause the death of the patient.

Pathology

The sites of the lesions can be grouped as follows :

A. Pelvic,

(a) Genital Tract :

1. Uterine :

(i) Diffuse.

(ii) Localized.

2. Extra-uterine:

(b) Extragenital.

B. Extra-pelvic.

On microscopical examination the essential feature is the appearance of the endometrial-like tissue, consisting of both glandular structures and stroma, in the various sites. The resultant picture varies considerably according to the tissue involved; for example, in the uterus there may be an accurate reproduction of normal endometrium, whereas in the ovary it may sometimes be impossible to find microscopical evidence of any recognizable endometrial tissue. The ectopic endometrium is usually responsive to the influence of the ovarian

hormones, and all variations may be seen ranging from the decidual reaction of pregnancy to the abnormal picture associated with cystic glandular hyperplasia. In other cases, there is no physiological response and the endometrium remains in the proliferative phase.

In the uterus itself the process may be either diffuse, when it is called adenomyosis, or more localized to form an adenomyoma. Adenomyosis often attacks one wall of the organ to a much greater extent than the other, giving rise to a slightly asymmetrical enlargement. The adenomyoma bears a superficial resemblance to the fibromyoma, but it has no capsule, its whorled and trabeculated cut surface does not show the circumscribed nodular arrangement of the fibromyoma, and it is frequently revealed by the tell-tale haemorrhagic or 'chocolate' spots, which are the endometrial islands scattered amongst the muscle fibres.

In the last thirty years or so a number of authors have described a rare condition known as stromatous endometriosis, in which there is invasion of the uterus, or occasionally of the ovary, by cells indistinguishable from the normal stroma of the endometrium; glandular structures are not found amongst these stroma cells. Apart from the microscopical appearance of the cells there seems to be little reason to consider this condition as allied to endometriosis. Although it has been described in younger women, many cases have occurred in patients over forty years of age and even in some women past the menopause. Indeed the onset of the menopause, either natural or induced, does not always cause regression of the condition. Cyclical bleeding into the abnormal cell masses does not occur, and menorrhagia rather than dysmenorrhoea is the main symptom. There is a tendency to form polypoidal masses which project into the cavity of the uterus. Spread to, and invasion of, tissues and structures in contiguity with the uterus may occur. Finally, local recurrence, sometimes after a long patent period, is not unknown and has in some cases resulted in the death of the patient. Park (1949) in an interesting paper on the subject suggests the use of some non-committal term like

Endometriosis of the ovary showing well-marked secretory change.

Endometriosis of the ovary showing an area of adenocarcinoma.

'stromatoid neoplasm of the myometrium.' But this is unlikely to compete with the more concise appellation at present used. Novak (1953), however, considers the condition to be a variety of adenomyosis, with the exception of the apparently malignant types, which he classifies as uterine sarcomata. Goodall (1944) also classified the condition as a type of endometriosis.

The extra-uterine sites in the genital tract include the ovaries, Fallopian tubes, uterine ligaments, peritoneum covering the tract, cervix, vagina and recto-vaginal septum. In the ovaries the chocolate cyst is the most notorious lesion. Chocolate cysts vary in size, but are seldom larger than 4 in. in diameter; they may be quite small and multiple; frequently they are bilateral. Because these cysts tend to perforate so that their contents leak outside the ovary, adhesions form around the sites of perforation and spread to contiguous structures follows. The appearances at laparotomy are fairly typical, in that the cystic ovaries are adherent to the posterior leaf of the broad ligament, with characteristic puckering of their surface, and there is an escape of tarry fluid as an attempt is made to free them. However, it is well to remember that not all chocolate cysts are due to endometriosis; haemorrhage can occur into any cyst of the ovary.

Peritoneal involvement is most commonly seen in the pouch of Douglas, when the uterus is found to be retroverted and fixed by dense adhesions to the rectum, which is drawn up, thus obliterating the pouch. Characteristic 'blueberry' spots, or tiny endometrial cysts, may be seen along the line of contact between the viscera. Elsewhere the lesions are seen as small endometrial cysts, either alone or in association with foci of nodularity, puckering and adhesions. In the uterosacral ligaments such nodular thickening is common and may be the first detectable physical sign of the disease. When the round ligament is involved a swelling may rarely appear in the groin. These ligamentous lesions are true adenomyomata and become swollen and painful during menstruation.

The rectovaginal septum is usually involved in association with extensive genital tract involvement elsewhere, but on occasion it is the main site. The lesion presents a fairly characteristic nodular, infiltrative thickening, which might, however, be mistaken for malignant disease of the rectum. The fact that endometriosis seldom erodes the mucosa of the bowel should help to distinguish between the two conditions, but it should be remembered that on rare occasions malignant change can supervene on the lesions of endometriosis.

The extragenital sites in the pelvis include peritoneum, bowel, in particular the sigmoid colon, and the bladder and ureters. In the bowel the

lesions may cause stricture formation and mimic malignant disease, but search should be made for signs of endometriosis elsewhere, for the tell-tale 'blueberry' spots and for the absence of involvement of lymph nodes, or of erosion of the mucosa. Cystoscopy will only be of value in endometriosis of the bladder late in the course of the disease, when grape-like cysts and 'blue folds of oedema' (Phillips, 1934) will be seen.

Extrapelvic sites include the umbilicus, laparotomy scars, hernial sacs, the bowel, the perineum and the vulva. More bizarre situations, such as the back of the thigh, the upper arm and the pleura have been authentically described, but they are exceedingly rare. The more superficial lesions present the characteristic tender swelling, which enlarges and becomes more painful during the menstrual period.

Symptoms

Due to the diversity of lesions, the symptomatology is equally diverse, but the most outstanding feature is pain. By far the commonest complaint is of severe, acquired and progressively increasing dysmenorrhoea: this dysmenorrhoea may have premenstrual congestive phase, but the most severe pain occurs during menstruation and has a tendency to persist throughout the period. Kelly and Schlademan (1949), who drew attention to this symptom, found acquired dysmenorrhoea in about 48 per cent. of 179 cases and progressive dysmenorrhoea in about 33 per cent. It is assumed that the pain is due to distension caused by menstruation of the enclosed ectopic endometrium. However, as has been noted above, the aberrant endometrium does not always respond to the ovarian hormones and yet these lesions may still be associated with considerable pain. Sometimes widespread pelvic endometriosis is found unexpectedly during laparotomies for other conditions, such as uterine fibromyomata, when no symptoms referable to endometriosis have been present; and, conversely, patients with little more than slight nodularity of the uterosacral ligaments and a little puckering of one ovary may have marked symptoms. This discrepancy between the extent of the involvement and the severity of the symptoms makes a rational explanation of the cause of the pain difficult. Other types of pain met with are constant backache, situated low down in the spine, pain around the rectum, both worse during menstruation, and deep dyspareunia. These symptoms are common with the classical lesions involving the ovaries, the pouch of Douglas and the uterosacral ligaments.

Whilst sterility, or relative infertility, is a common finding, it is seldom the main symptom. Infertility clinics do not seem to discover the early

stages of the disease amongst their clientele. Menstrual disorder is fairly common in endometriosis and is due either to pelvic congestion or, more likely, to a common underlying endocrine disorder. The more obvious methods of presentation in the superficial lesions have been mentioned. The most dramatic symptoms, such as cyclical haematuria or intestinal obstruction, occurring in conjunction with menstruation are rarely met. When the bladder is involved it is the base and trigonal region which is most often affected and increased frequency of micturition, dysuria and suprapubic pain are the usual symptoms. Whilst small bowel lesions may cause some degree of stricture formation, this seldom occurs in the more commonly affected sigmoid colon, and here the lesion is most often discovered at laparotomy for involvement of the genital tract.

Diagnosis

Despite the unusual nature of endometriosis, the correct pre-operative diagnosis is often overlooked. In Kelly and Schlademan's series only 14 per cent. of cases were correctly diagnosed. Whilst this difficulty is in part due to the fact that the condition may be relatively or completely symptomless, or be masked by coincidental disease, such as fibromyomata, it is often due to ignoring the possibility of its presence. It is a disease like pelvic tuberculosis, which needs to be borne in mind in the gynaecological clinic if it is to be correctly diagnosed more often. Acquired and progressive dysmenorrhoea in a sterile or relatively infertile woman about 30 years old should arouse suspicion. The presence of a fixed retroversion, or tender nodularity in the pouch of Douglas, is also suggestive of endometriosis. The final diagnosis can only be made, however, by surgical exploration backed up in most cases by histology. But there are times when the diagnosis has to be made solely on the macroscopical appearances at laparotomy, for microscopical evidence may be lacking, as is not infrequent in chocolate cysts of the ovary.

Treatment

Treatment presents many difficulties because the disease tends to be progressive until ovarian function ceases. Whilst this makes it relatively easy to cure older women and those not quite so old, who have yet managed to satisfy their reproductive ambitions, in the younger women, who, unfortunately, present the larger group, it means that permanent cure is unlikely at the first attempt. In the former group complete extirpation of ovarian tissue is all that is essential; this is, of course, usually combined with excision of the affected tissues. When bowel, bladder or rectovaginal sep-

tum are involved such surgical castration is sufficient to cause regression of the lesion and, provided malignancy has been excluded, resection is only necessary where stricture formation is present or imminent. In the younger age group conservative measures must be practised and reproductive function retained for as long as is reasonable. Whilst analgesics may suffice in the early stages, something more drastic is required before long. Surgical intervention in these circumstances is at best a piece-meal affair. Resection of diseased tissues must be undertaken with conservation of ovarian function; division of adhesions binding down the uterus, tubes and ovaries may aid conception; ventro-suspension will help to prevent further adhesions forming; presacral neurectomy is of value to relieve pain only for lesions which involve the uterus and uterosacral ligaments, but is valueless when the ovary is involved; finally, diathermy coagulation is some help for the discrete small foci scattered about the pelvis. Recurrence in these young women is to be expected, unless pregnancy follows. Although infertility is common in endometriosis, pregnancy does occur in a small number of cases, as Gainey *et al.* (1952) showed. Whilst it is true that many of these cases were only diagnosed presumptively, others were confirmed by operation and microscopical examination. These workers state that several of their cases showed marked subjective and objective improvement during pregnancy and that this improvement was sustained subsequent to confinement for periods ranging up to four years. A few patients successfully undertook further pregnancies. Kelly and Schlademan (1949) also report pregnancy following conservative operations for endometriosis in 23 per cent. of women who might reasonably have been expected to conceive. This possibility of conception, and the hope of the beneficial action of pregnancy, is the basis for conservative treatment and has led to the idea of inducing a pseudo-pregnant state by oestrogen therapy. Karnaky (1954), who has been advocating this method of treatment for some years, endeavours to keep his patients in a state of amenorrhoea for periods up to nine months. He uses micronized stilboestrol, starting with a dosage of 1 mg. per day and gradually increasing up to 100 mg. per day. Some patients require even larger doses to avoid bleeding. Karnaky claims striking results in that extensive lesions have disappeared and pain has been relieved. Haskins and Woolf (1955) also report good results in 15 cases treated along these lines and claim freedom from symptoms for periods up to two years following treatment. There still remains, however, widespread reluctance to use such large doses of oestrogens in this country and also in some quarters of the United States (Novak, 1956).

Testosterone is a more popular form of therapy in Great Britain, but in the main it can be only palliative in its action, for size and duration of dose must be limited by fear of unwanted side effects. It is noteworthy, however, that Macafee (1954) has caused complete resolution of a lesion in the perineum with testosterone. X-ray induction of the menopause is of value only when surgery has already been undertaken, as the diagnosis must of necessity remain presumptive until the abdomen has been explored. There are two types of case where such treatment is indicated, first in the older woman in whom complete extirpation of ovarian tissue has been impossible due to technical difficulties, and secondly in the younger woman who has a recurrence of symptoms following conservative surgical intervention, and for whom radiotherapy is preferred to a further difficult surgical venture.

The aetiology of the condition has been discussed at length by many authors and so will be mentioned but briefly here. The main theories are:

1. Cullen's direct invasion theory, which most authors agree accounts for many cases of adenomyosis uteri, although there are some who believe the myometrium capable of forming both glandular and stromal cells.

2. Sampson's implantation spill theory, which, after a period of rejection, is now again being more widely accepted, particularly in view of the experimental evidence furnished by Scott and Te Linde to show that in monkeys menstrual endometrium can implant in the abdomen and give rise to endometriosis.

3. Iwanoff's serosal metaplasia theory has many supporters and ingenious explanations are offered to explain all the reported lesions by this one theory. However, there seems to be no convincing explanation why there is never any transitional form seen and why the metaplasia should be so focal in nature and not more generalized.

4. Halban's lymphatic theory has few adherents; although lymph nodes have been found with endometrial structures in them, they are not common.

Whilst endometriosis is not a true neoplasm, it bears many close resemblances to one and therefore it might not be unreasonable to suppose that the spread of viable endometrial cells to ectopic situations could occur in a number of different ways and that, in differing circumstances, any one or more of the above theories might account for the various lesions of endometriosis.

I wish to thank Mr. A. J. Bailey for preparing the photomicrographs from material belonging to the Department of Pathology, Chelsea Hospital for Women.

BIBLIOGRAPHY

- GAINEY, H. L., KEELER, J. E., and NICOLAY, K. S. (1952), *Amer. J. Obstet. Gynec.*, **63**, 511.
 GOODALL, J. R. (1944), 'A Study of Endometriosis,' 2nd edition, Lipincott, Philadelphia.
 HASKINS, A. L., and WOLF, R. B. (1955), *Amer. J. Obstet. Gynec.*, **5**, 113.
 KARNAKY, K. J. (1954), *Mississippi Valley med. J.*, **76**, 187.
 KELLY, F. J., and SCHLADEMAN, K. R. (1949), *Surg. Gynec. Obstet.*, **88**, 230.
 MACAFEE, C. H. G. (1954), *J. Obstet. Gynaec. Brit. Emp.*, **61**, 348.
 MEIGS, J. V. (1949), *Surg. Gynec. Obstet.*, **89**, 317.
 NOVAK, E. (1953), 'Gynecologic and Obstetric Pathology,' 3rd edition, Saunders, Philadelphia, p. 222.
 NOVAK, E. (1956), *Obstet. Gynec. Survey*, **11**, 122.
 PARK, W. W. (1949), *J. Obstet. Gynaec. Brit. Emp.*, **46**, 759.
 PHILLIPS, R. B. (1934), *Ibid.*, **41**, 165.

RUTHIN CASTLE, NORTH WALES

A Clinic for the diagnosis and treatment of Internal Diseases (except Mental or Infectious Diseases). The Clinic is provided with a staff of doctors, technicians and nurses.

The surroundings are beautiful. The climate is mild. There is central heating throughout. The annual rainfall is 30.5 inches, that is, less than the average for England.

The Fees are inclusive and vary according to the room occupied.

For particulars apply to THE SECRETARY, Ruthin Castle, North Wales.

Telegrams: Castle, Ruthin.

Telephone: Ruthin 66