J Clin Pathol 1993;46:388–393

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ACP Broadsheet No 138 May 1993

Gross examination of uterine specimens

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Introduction

Gynaecological specimens form a substantial proportion of the workload in most departments. The aim of this broadsheet is to assist in the macroscopic description and handling of uterine specimens (table) to provide optimal sections for microscopic examination.

Uteri are best received unfixed, particularly in patients with cancer. Not only can appropriate tissue be selected and optimally processed for special investigations, including hormone receptors, electron microscopy, cytology imprints and some types of immunohistochemistry, but the fresh specimen is better for macroscopic description and preparation for demonstration at clinicopathological meetings and macrophotography. Endometrial autolysis occurs rapidly when incompletely opened or unopened uteri have been left in fixative in the operating theatre or laboratory. Formalin penetrates solid tissue very slowly from the exterior, and for practical purposes does not enter the uterine cavity. Tissue beyond a few millimetres from a formalin bathed surface autolyses before it fixes. Pre-warmed formalin is best not used to quicken fixation of uteri containing cancer as heat exacerbates the autolytic process of tissue not in contact with formalin. Endometrial curettings may be fixed in Bouin's solution, which gives better cytological preservation, particularly of the endometrial stroma.

Cervical specimens

ENDOCERVICAL POLYPECTOMY

Most cervical polyps are benign endocervical mucosal polyps. These are smooth surfaced, slippery, pedunculated and typically 1–2 cm in diameter. Small polyps are bisected and all are submitted. With large polyps, sampling is sufficient.

MANCHESTER REPAIR

Manchester repairs are performed for prolapse. The specimen consists of an amputated cervix, with one or two attached triangular fragments of vagina. These specimens are sent to pathology for audit purposes and present little diagnostic challenge.

CERVICAL PUNCH BIOPSY

Colposcopic cervical punch biopsy specimens are used to evaluate cervical intraepithelial neoplasia (CIN) and human papillomavirus (HPV) infection. Punch biopsy specimens are pale tissue fragments 2–3 mm in maximum dimension. They are completely transferred to the processing cassette, where they are protected from loss by being sandwiched between foam pads. Although there are techniques for orientation when cassetting, orientation is quite satisfactorily performed at the time of paraffin wax embedding. Levels should be cut.

CERVICAL WEDGE BIOPSY

These larger cervical biopsy specimens are taken to confirm an overtly invasive (at least stage 1b) cervical carcinoma before definitive treatment, or as an alternative to a punch biopsy specimen. Wedge biopsy specimens are up to 1 cm or more in maximum dimension, and should be measured as a surface area and a depth. They are sliced perpendicularly to the surface at 2–3 mm intervals, preferably in the long axis of the cervix. The long axis can be identified by the presence of longitudinal endocervical grooves.

Uterine specimens

Types of uterine specimens

Cervical specimens:
- Endocervical polypectomy
- Manchester repair
- Cervical punch biopsy
- Cervical wedge biopsy
- Cervical cone biopsy
- Large loop excision of the transformation zone (LLETZ)
- Endocervical curettings

Endometrial specimens:
- Endometrial curettings
- Uterine aspiration
- Endometrial resection

Myometrial specimens:
- Myomectomy

Hysterectomy specimens:
- No macroscopic abnormality
- Benign conditions
- Cervical intraepithelial neoplasia, past or present
- Cervical cancer
- Endometrial cancer
- Pelvic exenteration

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Accepted for publication 7 August 1992.

CERVICAL CONE BIOPSY

A cervical cone biopsy is performed to confirm and possibly treat microinvasive carcinoma or to investigate a high grade abnormal smear, where the lesion or the upper extremity of a lesion cannot be seen at colposcopy.

The diameter of the ectocervix, the measurements of the os, and the length should be recorded. The appearance of the ecto- and endocervical mucosa should be noted. There are several methods for dissecting a cone biopsy specimen. A common approach is to fix the cone whole, mark the stroma with ink or silver nitrate, then slice it parasagittally at 2–3 mm intervals, beginning at 3 o'clock or 9 o'clock (fig 1A). If the cone biopsy specimen is received fresh, an alternative method can be used. The cone is opened at 12 o'clock, pinned out, fixed for at least 2 hours, then divided into longitudinal strips at 0.2–0.3 cm intervals, beginning at 12 o'clock and progressing clockwise (fig 1B). Radial or coronal sectioning of the fixed cone are not recommended as the radial method can result in loss of epithelium and the coronal method does not give a good view of the transformation zone. Longitudinal blocks of cone biopsy specimens longer than 2.5 cm will not fit easily into a cassette whatever method is used. Long cones, whether arriving fixed or fresh, should therefore be shortened by having the apical, and if necessary, subjacent coronal blocks, taken before opening. The routine taking of a coronal apical block in normal sized cones, however, is not recommended, as coronal blocks give a tangential view of the resection line that is not as accurate as a perpendicular view given by longitudinal blocks.

LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE (LLETZ)

LLETZ biopsy specimens, taken under local anaesthesia are being increasingly used to diagnose and treat CIN.[1] The procedure involves removal of tissue by means of a diathermy effect generated at the end of a long wire loop. The resulting biopsy specimen is usually a cylindrical or coin shaped specimen consisting of ectocervix, endocervical canal, and stroma. The diameter of the biopsy specimen, the measurements of the os, and the length should be recorded. The biopsy specimen may have an orientating suture, usually marking the anterior lip. If so, the stroma of this half should be marked with ink or silver nitrate. There is no need to mark the resection lines as they can be identified histologically by looking for diathermy artefact. The biopsy specimen should be fixed whole and divided at 2–3 mm intervals into numbered parasagittal slices. Levels are not routinely cut.

Occasionally, tissue is removed in a stepwise manner resulting in numerous fragments termed cervical chippings. These should be weighed and all the material embedded. Where possible, fragments containing part (or the entire) cervical os should be identified and embedded separately. This will ensure that the squamocolumnar junction is adequately sampled.

Diathermy artefact in biopsy specimens derived using LLETZ can make handling and interpretation of the specimens troublesome, if not impossible. Difficulty in orientation of cervical chippings means that adequacy of excision cannot usually be commented on when tissue is removed in this manner.

ENDOCERVICAL CURETTINGS

Endocervical curettage is performed to evaluate the presence of intraepithelial neoplasia (squamous or glandular) in the endocervical canal. The curettings typically consist of a small quantity of mucus and blood in which strands of pale tissue can be seen. Like punch biopsy specimens endometrial curettings may be processed between foam pads. At embedding, the tissue fragments and residual mucus are picked out by fine forceps. Alternatively, the curettings may be processed wrapped up in filter paper, although, at embedding, there may be difficulty separating tissue strands from paper fibres.

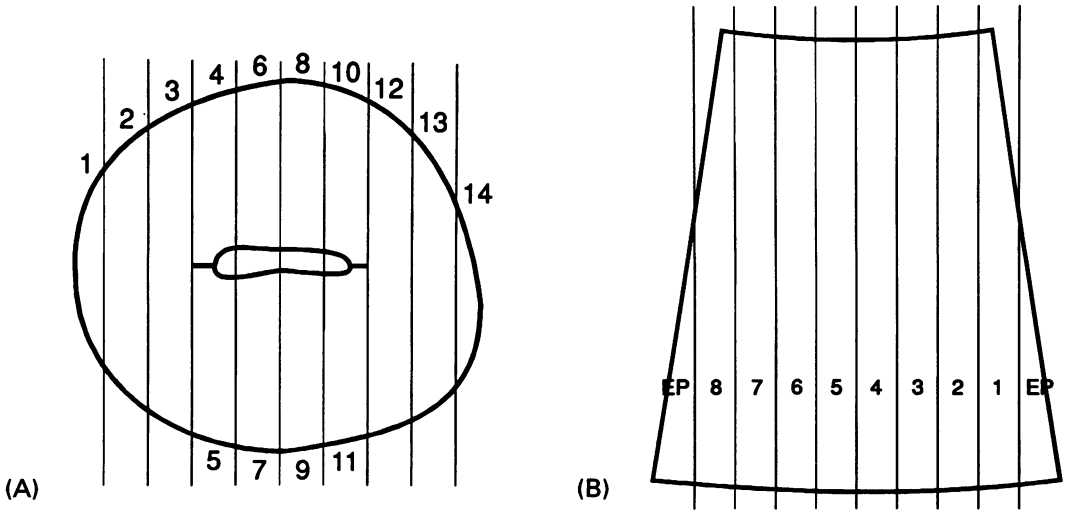

Figure 1 Methods for blocking of a cone biopsy specimen. (A) Parasagittal blocking of the whole fixed cone biopsy specimen. (B) longitudinal blocking of the opened, pinned out cone biopsy specimen (EP: End piece, usually not embedded).

Endometrial specimens

ENDOMETRIAL CURETTINGS

Endometrial curettage is performed in the investigation of abnormal uterine bleeding or infertility, or as a diagnostic and therapeutic procedure in abortion.

Non-gestational curettings

Normal endometrial curettings are strips of soft pink tissue mixed with blood clot and mucus. Their volume can be quite satisfactorily estimated in a semiquantitative way as small, medium, or large, or for the more obsessional, in cubic centimetres, or even weighed. Curettings derived from normal proliferative and early secretory endometrium seldom fill more than one cassette. If more than one cassette is required, late secretory endometrium, hyperplasia, malignancy or pregnancy should be suspected. Polypoid pieces may be identified in the curettings, but the definitive diagnosis of an endometrial polyp should await histological examination. Friable or firm yellowish tissue is abnormal and characteristic of endometrial carcinoma. If fat is identified macroscopically, it has most likely come from the peritoneal cavity through a uterine perforation, and the clinician should be warned of this possibility without delay. To exclude malignancy, all the curettings must be embedded.

Gestational curettings

In gestational cases the aim of the curettage is to confirm pregnancy and to exclude trophoblastic disease. A careful macroscopic search for products of conception looking for spongy tissue representing chorionic villi, a thin walled intact or disrupted cyst representing the gestational sac, and fetal parts is required. Products of conception per se are often outweighed by blood clot; dark red haemorrhagic thickened membranous tissue, with one shiny and one rough surface representing decidua and pink soft tissue, representing hypersecretory endometrium. In abortion abundant curettings are usually obtained; their quantity can be recorded by weighing. Only sampling, with emphasis on submitting probable products of conception, is practical. Two full cassettes are adequate, but if molar change is suspected further sampling should be undertaken.

ENDOMETRIAL RESECTION

Endoscopic resection of the endometrium is increasingly used as a treatment for dysfunctional bleeding. The aim of the procedure is to remove superficial and basal endometrium, leaving a base of myometrium so that menstrual bleeding is controlled or abolished. Endometrial resection specimens appear as multiple chunks of firm yellow and soft pink tissue, representing myometrium and endometrium. As with curettings, all the tissue should be embedded. Diathermy artefact may interfere with the reporting of these specimens, particularly as it tends to be most severe in superficial endometrium.

ENDOMETRIAL ASPIRATION

Another increasingly popular technique in gynaecological practice is the aspiration of endometrium through a tube or pipette. The main advantage of this procedure is that cervical dilatation and therefore anaesthesia is not required. The disadvantage is that the specimen is very small and may be unsatisfactory and contain no endometrium. A good aspirate specimen appears as a variegated core composed of tissue, blood, and mucus, of 2–3 mm in diameter and several centimetres long. These specimens are all submitted and processed between foam pads and reported like curettings.

Myometrial specimens

MYOMECTOMY

Myomectomy specimens are sent for histopathology to confirm the clinical diagnosis of leiomyoma and to exclude malignancy. Any deviation from the typical macroscopic appearance of a pale firm lesion with a white whorled cut surface should be noted and the abnormal tissue submitted for histological examination. Soft areas are particularly suspicious of malignancy. Myomectomy specimens should be weighed, measured, and sliced at 0·5 to 1 cm intervals. Routine sampling should include one block per leiomyoma, up to three blocks.

Hysterectomy specimens

The uterus should be weighed (after removal of adnexal structures), measured, and opened to expose the endometrium for adequate fixation. Note that the parous uterus (premenopausal adult 75–100 g) is heavier than the nulliparous uterus (premenopausal adult 30–40 g), and weight increases with parity, so that after eight pregnancies a weight of 240 g is normal.[2] Measurements for normal premenopausal adults are: length (top of fundus to ectocervix) 5–8 cm; width (intercornual distance) 3–5 cm; length and diameter of cervix both 3 cm.[2] The uterus may be orientated by (1) the "peritoneal" reflection being higher anteriorly to accommodate the bladder and (2) the observation that the round ligament is the most anterior, followed by the fallopian tube, followed by the ovary. The uterus may be impossible to orientate if it is grossly distorted by fibroids, or where much of the peritoneal surface is missing and no adnexal stumps are recognised, as occurs in some vaginal hysterectomy specimens. The uterus is first probed and then opened either anteriorly with incisions into the cornua or bisected laterally. Opening the uterus anteriorly is the more cautious approach and if this incision is used, care is required to expose fully the cornua. Uteri containing cancers should be either pinned out on a cork board or have cotton wool gently stuffed into the cornua before being placed in fixative. Opening the uterus laterally is quicker and the uterus opened in this manner can be placed directly into formalin, without further

attention. But unless care is taken during bisection, the knife may slip out of the plane of the uterine cavity.

NO MACROSCOPIC ABNORMALITY

It is recommended that the following blocks should be taken from a uterus with no macroscopic abnormality: two blocks of the full thickness of the cervix, including the squamocolumnar junction (anterior cervix and posterior cervix) and a variable number of blocks of full thickness of the corpus, usually two to four, depending on the length of the uterus; isthmus; body endometrium; and fundus endometrium (fig 2). All the blocks should be full thickness through the myometrium. If vaginal tissue is attached, it should be sampled. If the tubes and ovaries are attached, each structure should be sectioned. The ovaries should be bisected in their broadest plane passing through the hilum.

BENIGN CONDITIONS

If there are multiple leiomyomata in the uterus at least three of these should be sampled. If there is one large leiomyoma at least two blocks should be taken. Blocks of leiomyomata should always include the interface with myometrium as invasion of the myometrium is a helpful feature of malignancy. Any soft, necrotic, or haemorrhagic tissue should be submitted. Adenomyosis appears as whorling and thickening of the myometrium. Occasionally, small blue spots representing endometrium, are seen. Adenomyosis usually hugs the endometrial-myometrial border and extends for a variable distance into the myometrium. By contrast, an adenomyoma may be seen anywhere in the myometrium without any relation to the endometrium.

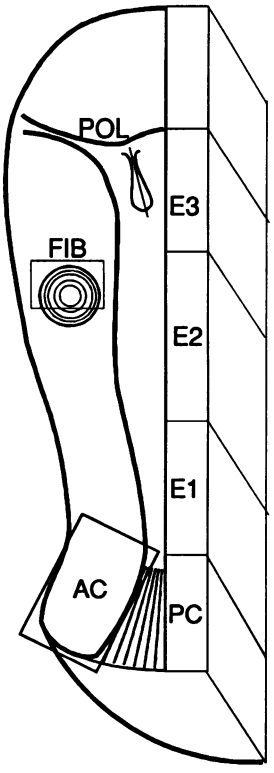

Figure 2 Routine blocking of the uterus (AC: Anterior cervix; PC: Posterior cervix; E1-E3: Endometrium; FIB: Fibroid; POL: Polyp).

Endometrial polyps can be smooth surfaced or papillary, sessile or pedunculated, soft or firm. Endometrial carcinoma sometimes begins in a polyp, and all polyps should be submitted in their entirety for histological examination.

CERVICAL INTRAEPITHELIAL NEOPLASIA, PAST OR PRESENT

In hysterectomy specimens of patients with a history of dyskaryotic smears or a current diagnosis of CIN, the cervix should be amputated and all submitted. The amputated cervix can be treated exactly like a cone biopsy specimen, but its larger size means more blocks will have to be taken. In cases of a history of CIN the yield of a positive diagnosis is low and a modification can be used to save time. In these cases the ectocervical resection line may be blocked tangentially before the remainder is sliced parasagittally (fig 3). When reporting, this modification will permit concentration on the squamocolumnar junction and ectocervical resection line.

CERVICAL CANCER

The usual surgical procedure for a cervical cancer is a radical hysterectomy and lymph node dissection. In young women the adnexae are often spared. A radical hysterectomy includes a vaginal cuff several centimetres wide, broad strips of parametria, and a variable proportion of the broad, round, and uterosacral ligaments.

The size, site, growth type, depth, completeness of excision should be noted about a cervical tumour.

Size: Measure in three dimensions and include the dimensions of the os.

Site: Large tumours are often circumferential. Smaller ones preferentially affect the anterior or posterior lips.

Growth: The tumour may be fungating, infiltrating, ulcerated or polypoid, or show a mixture of these characteristics. Necrosis and haemorrhage should be noted.

Depth: Recorded as depth of tumour infiltration or total cervical wall thickness.

Disease of the parametria: Macroscopic disease of the parametria is best assessed by slicing the cervix horizontally through 3 o'clock and 9 o'clock. Look for tumour extending

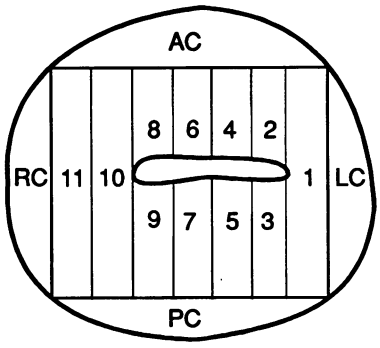

Figure 3 Blocking of the cervix in a hysterectomy specimen in cases of history of CIN. (AC: Anterior cervix: PC: Posterior cervix; RC: Right cervix; LC: Left cervix.)

through the full thickness of the cervical wall to reach parametrial fat.

Disease of vagina: Early disease can be difficult to assess as the fornices are often not apparent in the resected specimen.

Disease of the body of the uterus: Although corpus disease does not change the stage of a cervical cancer, it does worsen prognosis.

In a radical hysterectomy and lymphadenectomy specimen it is difficult to avoid taking numerous blocks. Where possible, economy should be exercised. The circumference of the vaginal resection line can be blocked in strips in one or two cassettes. Note that sometimes in advanced tumours the vagina may be affected by tumour in submucosal lymphatic channels, while the mucosa remains normal. With a macroscopic tumour, as a minimum, the tumour should be sampled by a full thickness block from each of the four quadrants. If a tumour is longer than a cassette then four additional blocks from the upper endocervix or isthmus should be added. The remainder of the cervix is then carefully longitudinally sliced, looking for more deeply invasive tumour. The anterior and posterior blocks can be used to assess the anterior (bladder) and posterior resection lines, which can be inked. The blocks from the right and left sides of the cervix are used for assessment of the degree of disease in the parametrium, and these two blocks should include some inner parametrium. It is usually not worth inking the parametrial resection lines if the parametria include a thick cuff of normal looking fat. In some specialist centres the entire cervix is blocked in cases of cervical cancer. If a tumour cannot be found macroscopically, then this is mandatory. In large cervical tumours a good overview of the tumour and the resection lines can be obtained in oversized blocks, which are hand-processed and cut on a sledge microtome. Unfortunately, this excellent technique is out of favour in many pathology departments because it requires special equipment and is so time consuming. The remainder of the parametrium should be sampled by parallel slices, beginning closest to the cervix and paying particular attention to sample any thickening or induration. Small lymph nodes may be identified in the parametrium. The remainder of the uterus and, if present, the adnexae should be sampled according to the "benign conditions" protocol. In cases of adenocarcinoma of the cervix, particularly adenoma malignum, attention should be paid to the ovaries as there is an association with mucinous tumours of the ovary.

The number of lymph nodes affected by metastases and their location is of crucial importance to the clinician and determines whether postoperative radiotherapy will be given. Lymph nodes from cases of cervical cancer will arrive in the laboratory in labelled pots. It is helpful to arrange and number the pots in a logical order, with right and left next to each other (fig 4). All lymph node tissue should be embedded. The only exception to this rule is when a large node shows obvious tumour in which case sampling will suffice. It is permissible to put more than one lymph node in each cassette, but it is counterproductive to stuff the cassette with fatty tissue, which will inevitably process poorly. If a lymph node has been sliced, then all pieces should be placed into one cassette if possible. A large node may require two or more cassettes. The number of lymph nodes embedded in each cassette should be recorded. A single deep level, as well as the standard section cut from each lymph node block, will increase the yield of metastases.

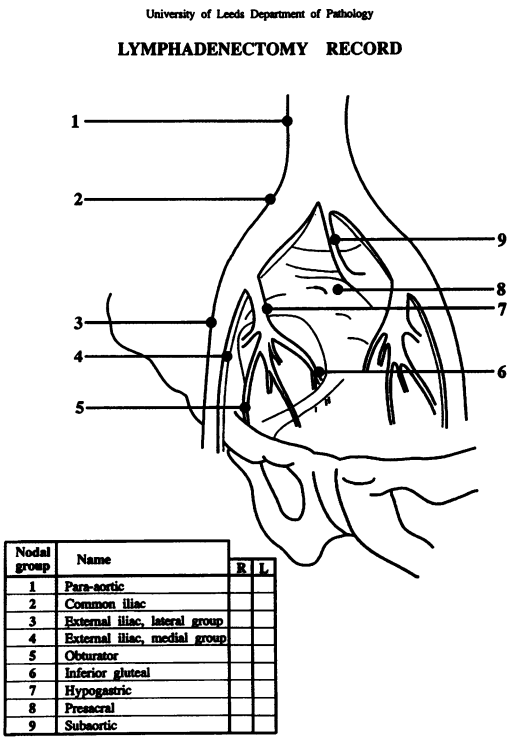

Figure 4 Guide to blocking lymphadenectomy specimens in uterine cancers.

ENDOMETRIAL CANCER

A protocol for the histopathological reporting of endometrial carcinoma is shown in fig 5. The location, size, growth pattern, and extent of myometrial and cervical disease should be recorded from macroscopic examination of an endometrial carcinoma.

Location: The tumour may be from the fundus, body, isthmus, cornu, and be from the right or left side, anterior or posterior.

Size: Measure in three dimensions in centimetres.

Growth pattern: The tumour may be solid or papillary or a mixture of these patterns, and may be ulcerated, necrotic, or haemorrhagic.

Myometrial invasion: To assess the deepest point of myometrial invasion the uterus should be cut in parallel slices, virtually full thickness, but with the serosa intact, so that the uterus is still hanging together. Measure maximum depth of myometrial invasion, the overall thickness of the myometrium, and the minimum distance of the tumour from the serosal surface in millimetres.

Cervical spread: Cervical disease changes the stage of corpus cancer. Direct spread is easily

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Protocol for the Pathological Reporting of Endometrial Adenocarcinoma

UTERUS: Weight: ..... g (without appendages)
Dimensions: .....

TUMOUR:
Solid ☐
Papillary ☐
Ulcerated ☐
Necrotic ☐
Haemorrhagic ☐

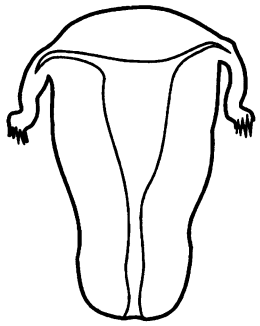
Tumour size: ..... cm.

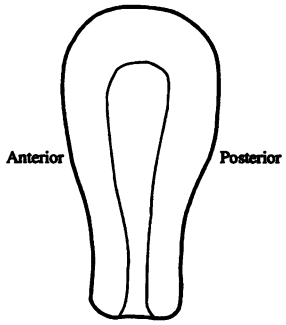
Is the endocervix involved by tumour? YES NO

Is there myometrial invasion? YES NO

<1/3 ☐ >1/3 ☐ >2/3 ☐

Overall thickness of myometrium ..... cm
Depth of invasion ..... cm
Minimum distance of tumour from serosal surface ..... cm





ADNEXA

	Normal	Abnormal (specify)	Lymph nodes (specify group and number
Right ovary	☐		
Left ovary	☐		
Right tube	☐		
Left tube	☐		

COMMENTS

Figure 5 Protocol for the pathological reporting of endometrial adenocarcinoma.

seen, but metastases to the endocervix are also quite common. These can be deceptively small and innocent looking and may appear as small, congested, or haemorrhagic polyps.

Blocks of the tumour should be full thickness through the uterus so that the depth of myometrial invasion can be assessed histologically. Blocks should be labelled to indicate where they are taken from. If the myometrium is too thick for a single cassette, use two cassettes with appropriate designation. Apart from sampling of the tumour, block taking from a uterus with an endometrial cancer should follow the routine outlined above. Lymph nodes should be handled in the same way as cervical carcinoma.

PELVIC EXENTERATION

Pelvic exenterations may be of three types: total, anterior, or posterior. Total pelvic exenteration includes the uterus and adnexae, bladder and distal ureters, anorectosigmoid colon and pelvic peritoneum. Anterior exenteration excludes the anorectosigmoid; posterior exenteration excludes the bladder. Although performed in late stage disease, pelvic exenteration is used as a curative procedure, not for palliation. Special consideration should be given to the various resection lines and invasion of the rectum or bladder by tumour.

1 Mor-Yosef S, Lopes A, Pearson S, Monaghan JM. Instruments and methods: Loop diathermy cone biopsy. *Obstet Gynecol* 1990;75:884–6.
2 Robboy SJ, Kraus FT, Kurman RJ. Gross description, processing and reporting of gynecologic and obstetric specimens. In: Ferenczy A, ed. *Blaustein's pathology of the female genital tract.* Third edn. New York: Springer Verlag 1987:925–40.