is normal, and surgical debridement the exception. Accordingly, the consequences may be only appreciated in a subsequent pregnancy. If the patient does present before this, hemorrhage and/or vaginal discharge may prompt internal examination. A defect may be identified on palpation. Curettage may be undertaken and may retrieve inflammatory exudate, degenerating decidua, polypoid endometrium or fragments of necrotic myometrium that have prolapsed into the endocervical lumen from the internal edge of the Cesarean section scar. Sometimes, quite large pieces of myometrial tissue with edema and coagulative necrosis are obtained. This myonecrosis, or incisional necrosis, is caused by local ischemia[4]. Remodelling of blood vessels may influence implantation. Implantation on either a normally healed or on a diseased scar will not have the protective effect of the decidua vera (see below), and so postpartum separation is less likely to occur. A Cesarean section at first birth is associated with increased risks of placenta previa and abruption in second pregnancies[5].

Implantation in the lower segment (adjacent to the defect) can cause expansion of the defect, dehiscence of the wall and the formation of a pulsion diverticulum which will further enlarge and progress with growth of the placenta. If the implantation is fundal, a fortuitous elective section may reveal a thin, almost transparent anterior lower segment wall. This should be more easily resected at closure since the scar will not be excessively vascular. If implantation is in the lower segment or in the scar, then there is a potential for catastrophic hemorrhage on attempt at delivery of the placenta.

In examining a postpartum hysterectomy specimen where there is a history of previous Cesarean section, the points noted above should be borne in mind. The recently sutured section incision should be carefully reopened. Following photography, the edges and margins should be inspected for thinning and scar tissue formation. An enlarged, ragged and open defect of the anterior lower uterine segment, now tightly contracted and rigid with formalin fixation, may be all that is left of a huge, thin-walled, placenta-filled diverticulum, the result of scar dehiscence and rupture. It is easy to destroy this thin structure with precipitate dissection. Examination of the lateral margins of the defect may indicate left- or more often right-sided extension of the bulging diverticulum into parametrial soft tissue of the pelvis. A complete section through the anterior lower uterine segment can identify previous Cesarean section scars with tenting defects and the shape and edges of a recent section. Most importantly, en-face examination of the lateral sides of the lower segment will show the cavity and lateral extension of a dehiscence diverticulum, fresh tears and/or adherent placenta. The issue of abnormal adherence is addressed below.

FUNDUS

Important pathologies include retained products, placenta creta, and subinvolution. Placenta creta is the name given to abnormally adherent or ingrowing placenta that does not detach with full contraction of the uterus after expulsion of the fetus. This term covers placenta accreta (abnormal attachment to the wall), increta (extension of villi into the myometrium) and percreta (extension of villi through to the serosa). The intimate relationship of villous tissue to myometrium, without intervening decidua, is the key to the diagnosis. Descriptions of placenta percreta based on illustrations or descriptions of chorionic villi displaced between torn myometrial fibers should be evaluated critically.

MRI may show the loss of zonation associated with penetration rather than invasion of chorionic villi.

Full-thickness anteroposterior sections of the fundus make it easier to recognize the position of the contracted placental site. It is surprisingly difficult to identify the exact site on inspection of the raw decidual surface that is seen if the uterus is opened laterally.

Detachment of the placenta is dependent on the presence of a normal spongy decidua vera, where shearing of the placenta from the myometrium occurs. This soft compressible area is not seen when the postpartum uterine lining is examined histologically, because its many mucous glands are disrupted to facilitate the normal plane of cleavage. It is seen to its full extent in the tragic case of maternal death prior to labor. Either Alcian blue stain or diastase-PAS to

demonstrate mucopolysaccharides in the swollen gland crypts can help to identify this layer. Deficiency of this layer may be focal or, rarely, complete. When it is absent, the thinned Nitabuch's layer with anchoring villi lies in close proximity to muscle fiber bundles or interstitial fibrous Cesarean section scar. An occasional finding is the presence of abundant intermediate trophoblast infiltrating between muscle fibers beneath a firmly adherent Nitabuch's layer. Histological examination of multiple sections can show anchoring villi penetrating Nitabuch's fibrinoid and ghost villi in dense fibrin adherent to muscle. The often described appearance of chorionic villi infiltrating between muscle fibers is characteristic only of invasive mole; the key to placenta percreta is absence of decidua. An increased number of implantation site intermediate trophoblasts has been shown in cases of placenta creta compared with controls[6]. Retained placental fragments reflect some degree of placenta creta and are more common in women with a spectrum of changes in previous pregnancies, such as pre-eclamptic toxemia, growth restriction, spontaneous abortion and retained placental fragments. It has been hypothesized that these reflect abnormal maternal–trophoblast interaction[7].

Placenta creta is therefore due to a deficiency of the decidua. The end result of penetration of the placenta though a weakened part of the uterine wall includes rupture and secondary changes, including serosal peritoneal reaction. Curette penetration may cause secondary infection or hematoma formation and provide the nidus for dehiscence into the adherent bladder wall, if this had been injured at previous surgery.

Placenta creta is only part of the problem of uncontrolled postpartum hemorrhage. The thin myometrium, with little muscle, interstitial fibrosis and increased intermediate trophoblast will contain large dilated arteries of pregnancy and often widespread extrauterine extension of these changes into the parametrium, as described on Doppler ultrasound. The degree of constriction–contraction of the myometrium is insufficient to close off these vessels. Where there is severe thinning of the muscle of the lower segment with diverticulum formation, abnormal adhesion is not necessary to sustain bleeding. Conversely, on histological examination of the lining of the postpartum uterus, the finding of chorionic villi in clefts in the placental bed may be an artefact rubbed in following clearance of uterine contents and is of no diagnostic consequence. Smearing of DNA due to crush artefact may be helpful in distinguishing this from true extension.

RETAINED PRODUCTS OF CONCEPTION

The failure of total expulsion of the placenta may lead to postpartum hemorrhage. A fragment of placenta remains, assumes a polypoid shape ('placental polyp'), and undergoes compression and devitalization. Some viable cells may remain in stem villi. Vessels below the retained fragments may show persistent dilatation. There may be a plasma cell infiltrate in the adjacent myometrium – this is not diagnostic of (infective) endometritis in this context. The frequency of detection of retained products varies from 27 to 88%[7], but much of this literature is decades old. Retained placental fragments are more common in women who have had complications such as pre-eclampsia or growth restriction in previous pregnancies. This has been interpreted as indicative of an abnormal maternal–trophoblast relationship[7].

SUBINVOLUTION

Subinvolution of the blood vessels of the placental bed, in the absence of retained placental fragments, is an important and distinctive cause of secondary postpartum hemorrhage.

Normal arterial involution involves a decrease in the lumen size, disappearance of trophoblast, thickening of the intima, re-growth of endothelium and regeneration of internal elastic lamina. These changes occur within 3 weeks of delivery. With subinvolution, arteries remain distended and contain red cells or fresh thrombus, and trophoblast persists in a perivascular location[8]. In some cases, endovascular trophoblast may be present. Hemorrhage from subinvolution is maximal in the second week postpartum, although it may occur up to several months later. It is commoner in older, multiparous women and may recur in subsequent deliveries.

Subinvolution is not related to the method of delivery and may be regarded as a specific entity, possibly due to an abnormal immunologic relationship between trophoblast and the uterus[8]. Despite this, it did not show the association with markers of such an abnormal relationship seen with retained placental fragments in another study[7].

The changes may be recognized on curettage specimens. The hysterectomy specimen will show a uterus that is soft and larger than expected[8]. As normally involuted vessels may be present adjacent to subinvoluted ones, multiple blocks of placental bed should be taken to exclude this process.

ATONY

This is well-recognized obstetric phenomenon, but there may be relatively little to report in the way of pathology. The diagnosis is one of exclusion. The uterus is enlarged, edematous and soft, with edema and hemorrhage apparent microscopically. The diagnosis will depend on clinical information, combined with adequate histologic sampling to exclude other causes.

ARTERIOVENOUS MALFORMATIONS

Uterine arteriovenous malformations (AVMs) are rare and may present with profuse hemorrhage, including hemorrhage in the postpartum period. Congenital AVMs consist of multiple small connections and may enlarge with pregnancy. The more common acquired AVMs are rare in nulliparous women, and are thought to arise following uterine trauma: curettage, myomectomy or even previous uterine rupture[9,10]. AVMs may co-exist with retained products of conception or trophoblastic proliferation. Pathologically, vessels of arterial and venous caliber are present, along with large vessels of indeterminate nature.

OTHER CAUSES

Lacerations of the inner myometrium have been reported to cause postpartum hemorrhage[11]. Women with leiomyomas are at an increased risk of postpartum hemorrhage[12]. Less commonly, endometrial carcinomas and congenital anomalies may also result in reduced decidua formation and subsequent postpartum hemorrhage. Trophoblastic disease has also been reported in this context.

ENDOMETRITIS

An acute endometritis is reported as a cause of sepsis and postpartum hemorrhage. It is relatively uncommon in modern obstetric practice in the West and may be due to a variety of organisms. It accounted for < 5% of cases of delayed postpartum hemorrhage in one series[7].

PLACENTAL PATHOLOGY

The placenta should be examined in cases of postpartum hemorrhage. Pre-eclampsia may cause retroplacental hemorrhage: recent and old hemorrhages and infarcts may be seen. The characteristic changes of acute atherosis are only present in 50% of cases of pre-eclamptic toxemia. However, examination of the parenchyma will usually show so-called accelerated villous maturation (distal villous hypoplasia) in response to uteroplacental ischemia. Sampling from the center of the disc is important to avoid overinterpretation of physiologic changes[13].

THE AUTOPSY IN POSTPARTUM HEMORRHAGE

In data drawn from the Confidential Enquiries into Maternal Deaths in the UK for the period 1970–90, approximately 10% of direct maternal deaths are due to hemorrhage[14]. Roughly half were antepartum and half postpartum. Excess blood loss is more common in older women (> 35 or 40 years, depending on the study)[15].

Before beginning an autopsy in a case of maternal death following postpartum or intrapartum hemorrhage, it is critical to plan the procedure and the sequence of the autopsy in the light of the information received and the suspected cause or causes and mode of death. The autopsy must be unhurried and methodical; it is a fundamental mistake to seek to demonstrate immediately the proposed cause of death. Members of the clinical team should be asked to attend the autopsy, but it is unwise to have everybody there during what will be a long

phase of inspection, measurement and initial systematic dissection. When all is ready, the procedure is stopped and members of the team attend. In this way, the history can be reviewed, pre-existing conditions or disease discussed and demonstrated, e.g. chronic pyelonephritis, and the dissection and demonstration of the focus of main clinical interest can begin.

A fundamental aspect of good autopsy practice is the confident exclusion of specific diseases and conditions in a systematic approach. The understandable desire and pressure to skip to the seat of disease must be resisted. The parametrium, pelvic side-wall and vagina are as important objects of attention as the uterus.

At the time of external inspection of the body, the pathologist must consider in turn each of the major causes of maternal death. Many require modification of routine techniques, e.g. air embolism, amniotic fluid embolism, ruptured aneurysm, and these modifications are detailed elsewhere[16]. Preparation and sampling of blood and fluids for hematology, hemophilia, toxicology and microbiology should be planned, e.g. sample containers should be pre-labelled and set out in sequence. Cardiopulmonary resuscitation attempt most likely preceded death and therefore the features and sequence of sustained unsuccessful resuscitation must be identified and complications and agonal changes interpreted in this context. It is important from a medicolegal aspect not to allow such artefact to be construed as a major factor in the cause of death, e.g. liver or mesenteric tear, blood in the abdomen, bone marrow embolus.

The traditional Y-shaped autopsy incision should be extended to an abdominal inverted Y with the incision continued to the inguinal femoral triangle on each side. This allows better examination of the ileofemoral vessels and better exposure of the pelvis. Blood and blood clots are removed from the abdomen and the amounts measured. The relative size and position of the abdominopelvic organs are assessed. The peritoneal lining of the pelvis is inspected, noting color, texture and degree of congestion. Patches of peritoneal decidual reaction of pregnancy can be identified by their gelatinous appearance.

In traditional autopsy practice, the state of pregnancy can be suspected, even when the uterus is still small, by the characteristic dilated and congested appearance of retroperitoneal veins. The degree of dilation and turgidity of the pelvic veins should be noted at autopsy as they will be dissected and examined in detail later. Retroperitoneal hematoma and broad ligament hematoma should be identified or excluded at this stage as these may be less easily assessed and measured following organ removal. The uterus may be examined and opened *in situ*, but it is better to remove adrenal, renal and pelvic organs as one complete block.

The traditional method of blunt dissection along the pelvic side-wall and pubis with transection at the mid to upper vagina is extended in the investigation of postpartum hemorrhage. Following knife separation of the symphysis pubis, the legs are externally rotated and a knife cut is made along the lower edge of the pubic bone. The pubic bones are forcefully separated by 8–10 cm. This, together with the inguinal femoral incisions, gives good exposure of the paracervical and paravaginal soft tissues. Lateral vaginal wall tears and hemorrhage can be inspected and well demonstrated by this modified technique. The ileofemoral vessels are transected and inspected. The complete urogenital block is placed on a dissection board where it can be opened in layers, beginning with the urethra and bladder, then the vagina and cervix. Alternatively, the block can be placed in formalin and later dissected after short fixation.

The aorta is opened posteriorly and incision is extended into the branches of the iliac arteries for a short distance. The inferior vena cava is opened from the anterior side, probed and dissected into the right and left renal veins; the ovarian veins are identified and opened and dissection is continued into the branches of the pelvic veins out to the limits of the excised specimen. The intima is examined for evidence of tear or abrasion and for adherent thrombus. Pieces of tissue containing venous plexus from the broad ligament and parametrium are selected for formalin fixation and histological examination.

When the patient has died of hemorrhage and where there has been attempt to stem the bleeding by hysterectomy and under-sewing of bleeding sites and pedicles, it may be very

difficult to identify the exact sites of bleeding, and ancillary techniques may be helpful. Prior to pelvic dissection, an infusion of saline through an intravenous infusion set and cannula into the clamped abdominal aorta can identify a bleeding point. With special preparation and ligation of all peripheral vessels, post-mortem specimen angiography may be very valuable in selected cases.

The most useful of all techniques is the histological examination of carefully selected blocks of tissue demonstrating vital reaction to injury and the presence or absence of conditions predisposing to disease.

References

1. Schaaps JP, Tsatsaris V, Goffin F, *et al*. Shunting the intervillous space: new concepts in human uteroplacental vascularisation. *Am J Obstet Gynecol* 2005;192:323–32
2. Cheung ANY, Luk SC. The importance of extensive sampling and examination of cervix in suspected cases of amniotic fluid embolism. *Arch Gynecol Obstet* 1994;255:101–5
3. Morris H. Surgical pathology of the lower uterine segment caesarean section scar: is the scar a source of symptoms? *Int J Gynecol Pathol* 1995;14:16–20
4. Rivilin ME, Carroll CS, Morrison JC. Uterine incisional necrosis complicating caesarean section. *J Reprod Med* 2003;48:687–91
5. Getahun D, Oyelese Y, Salihu H, Anath CV. Previous caesarean delivery and risks of placenta previa and placental abruption. *Obstet Gynecol* 2006;107:771–8
6. Kim KR, Jun SY, Kim JY, Ro JY. Implantation site intermediate trophoblasts in placenta cretas. *Mod Pathol* 2004;17:1483–90
7. Khong TY, Khong TK. Delayed postpartum hemorrhage: a morphologic study of causes and their relation to other pregnancy disorders. *Obstet Gynecol* 1993;82:17–22
8. Andrew AC, Bulmer JN, Wells M, Morrison L, Buckley CH. Subinvolution of the uteroplacental arteries in the human placental bed. *Histopathology* 1989;15:395–405
9. Grivell RM, Reid KM, Mellor A. Uterine arteriovenous malformations: a review of the current literature. *Obstet Gynecol Surv* 2005; 60:761–7
10. Ciani S, Merino J, Vijayalakhsmi, Nogales FF. Acquired uterine arteriovenous malformation with massive endometrial stromal component [letter]. *Histopathology* 2005;46:234–5
11. Hayashi M, Mori Y, Nogami K, Takagi Y, Yaoi M, Ohkura T. A hypothesis to explain the occurrence of inner myometrial laceration causing massive postpartum hemorrhage. *Acta Obstet Gynecol Scand* 2000;79:99–106
12. Qidwai GI, Caughey AB, Jacoby AF. Obstetric outcomes in women with sonographically identified uterine leiomyomata. *Obstet Gynecol* 2006;107:376–82
13. Mooney EE, Padfield J, Robboy SJ. Nidation and placenta. In Robboy SJ, Anderson MC, Russell P, eds. *Pathology of the Female Reproductive Tract*. London: Churchill Livingstone 2002:721–57
14. Toner PG, Crane J. Pathology of death in pregnancy. In Anthony PP, MacSween RNM, eds. *Recent Advances in Histopathology*, Vol 16. Edinburgh: Churchill Livingstone 1994:189–212
15. Ohkuchi A, Onagawa T, Usui R, *et al*. Effect of maternal age on blood loss during parturition: a retrospective multivariate analysis of 10,053 cases. *J Perinat Med* 2003;31:209–15
16. Rushton DI, Dawson IMP. The maternal autopsy. *J Clin Pathol* 1982;35:909–21