MY APPROACH

My approach to performing a perinatal or neonatal autopsy

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An opportunity to determine the cause of death, factors that may have a role in it, and the extent and cause of malformations is provided by perinatal autopsy. The family may be assisted in finding closure after the death of their infant by the information obtained. Insight into classifying infants appearing normal into one of three groups, small, appropriate and large for gestational age, has been provided, as each group tends to have specific causes of death. In infants with congenital anomalies, patterns of malformation may lead us to the diagnosis. An accurate diagnosis is required to provide counselling for a subsequent pregnancy.

Perinatal autopsy provides an opportunity to determine the cause of death, factors that may have a role in it, and the extent and cause of malformations.

PRE-AUTOPSY CHECKLIST

Preparation

Before starting the autopsy, check the type of consent given, the identity of the infant and consult the clinicians, to determine the questions that have to be answered by the autopsy.

Imaging

A radiograph of the whole body is helpful. Postmortem arteriography is advocated only if a vascular abnormality is present.¹ Abnormalities shown by radiography ranged from 9% to 30%^{1–3} and provided a diagnosis in 0.9% of cases.³ Ossification centres provide a rough index of bone maturation.⁴ Metaphysitis of the long bones may be seen in congenital infections such as syphilis, and cerebral calcification in toxoplasmosis and cytomegalovirus infection. Radiographs may also show abdominal or vascular calcification, which may be calcification of the arterial walls or venous thromboses.^{5–8} If there has been trauma, radiography of the skull and limbs is essential.⁹ In skeletal dysplasia, radiography forms a major part of the diagnosis,¹⁰ and lateral views and views of the hands and feet should also be taken.

A correlation of the findings of postmortem examination with those of ultrasound assessment is required and has ranged from 46% to 72%,^{11–13} with the postmortem examination providing an audit on the standard of ultrasonography.¹⁴ Early cardiac ultrasonography of unselected fetuses is not advisable.¹⁵ In fetuses with increased nuchal lucency, however, cardiac ultrasonography at 12–16 weeks showed a

cardiac abnormality, either structural or functional, in 22% of cases, and an abnormal karyotype in 8%.¹⁶ A recent study from Norway described congenital cardiac defects that were missed on ultrasonographic screening and clinically at birth, and were diagnosed only after a second admission.¹⁷

Magnetic resonance imaging (MRI) has been used for detecting malformations of the central nervous system (CNS) and neuronal migration disorders, as well as to study the development of myelination.^{18–21} A prolongation of relaxation times in the neonate occurs because of the high water content in the brain. High-resolution multiplanar MRI provides good anatomical delineation and distinction between grey and white matter. Where consent for an autopsy is refused, it provides a good alternative for examination of the brain and may detect abnormalities of the CNS that are not seen at postmortem examination.²⁰ Low-field dedicated MRI is a potential tool in perinatal autopsy²² (figs 1, 2). A detailed MRI study of malformations of the CNS, combined with postmortem examination and frozen tissue storage for DNA studies, has led to the detection of mutations of genes that are responsible for malformations. This has led to prenatal diagnosis on chorionic villous biopsy at 10–12 weeks of gestation.²¹ Comparison between ultrasound and MRI of a series of 100 cases with abnormalities of the CNS showed concurrence in 52 cases, and 35 cases in which additional information provided by MRI altered the management of the case.²³

Full body, face and facial profile photographs help in diagnosis and can be used for consultation. Digital photographs are particularly useful. A black and white print can be kept with the paperwork of the autopsy, providing for easy comparison with reference books. Photographs of malformations are essential.

Metabolic case

If a metabolic disorder is queried, tissue samples need to be taken within 4–6 h of death. Skin for fibroblast culture should be placed in growth media at room temperature. Muscle, heart, brain and liver should be snap frozen and taken for electron microscopy. Plasma, blood and urine should be frozen. Bile and blood should be stored on filter paper at room temperature. Other tissues that may be used include conjunctiva, intestine, peripheral nerve, bone marrow and amniocytes.^{24–25}

Abbreviations: CNS, central nervous system; MRI, magnetic resonance imaging

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Figure 1 Diagnostic algorithm for perinatal autopsy. abruptn, abruptio; accel mat, accelerated maturation; ac, acute; AGA, appropriate for gestational age; asphyx, asphyxia; asym, asymmetrical; CHD, congenital heart disease; chorioam, chorioamnionitis; chr, chronic; CMO, cardiomyopathy; compress, compression; CVS, cardiovascular system; diab, diabetic; DM, diabetes mellitus; hypoglyc, hypoglycaemia; hypotherm, hypothermia; hypox, hypoxia; HMD, hyaline membrane disease; IDM, infant of diabetic mother; inf, infection; insuff, insufficiency; intrapart, intrapartum; IUD, intrauterine death; IUGR, intrauterine growth retardation/restriction; IVH, intraventricular haemorrhage; LGA, large for gestational age; malf, malformation; matern, maternal; memb, membrane; MPFD, massive perivillous fibrin deposition; N, normal; NEC, necrotising enterocolitis; NND, neonatal death; NTD, neural tube disease; prem, premature; pulm haem, pulmonary haemorrhage; PVL, periventricular leucomalacia; SGA, small for gestational age; skel, skeletal; syncyt, syncytial; traum deliv, traumatic delivery; typ pla, typical placenta; vasc dis, vascular disease; vasculop, vasculopathy; ven throm, venous thrombosis; unexpl, unexplained; ut, uterine.

PERFORMING THE AUTOPSY

External examination

Morphometry

Measurements of crown heel, crown rump, head circumference, foot length and weight are taken for comparison with standard charts. Wigglesworth provides weights and measurements for stillborn and liveborn infants by using data from the Women & Infants Hospital, Providence, Rhode Island, USA. Foot length is used to determine gestational age, which can then be compared with chronological age. The infant can be classified as small, appropriate and large for gestational age.²⁶⁻³⁰ Measurements of crown heel and head circumference should be equal. A discrepancy of 20 mm

indicates microcephaly or macrocephaly, or a disproportionate body. The biparietal diameter can be directly compared with ultrasonographic measurements. With facial dysmorphism, inner and outer canthal distances, interpupillary distance and length of palpebral fissures³¹ are helpful. Systemic examination of the infant is conducted by using a checklist.

Head and skull

After a forceps or vacuum extraction, the infant is examined for abrasions, cephalhaematoma or subaponeurotic haemorrhage. Dissection of the suboccipital region is essential before opening the skull.³² Bulging fontanelles indicate intracranial

Figure 2 Investigative tree for infants with arthrogryposis phenotype, indicating lack of adequate movement in the uterus. Congen, congenital; CNS, central nervous system; dermatopath, dermatopathy; Holoprosen, holoprosencephaly; Hydranenceph, Hydranencephaly; Inflamm myositis, inflammatory myositis; Met myopathy, metabolic myopathy.

disorder. The presence of additional fontanelles or defects of the skull raises the possibility of a chromosomal defect or Meckel–Gruber syndrome, where an encephalocele is a frequent finding. Splayed sutures suggest hydrocephalus, and premature fusion of the sutures indicates craniosynostosis, where there is an abnormally shaped head, small fontanelles and proptosis owing to shallow orbital fossae. Defects of the scalp are seen in trisomy 13.

Skin

Multiple haemangiomas suggest Osler–Rendu–Weber syndrome and leaf-shaped café au lait spots tuberous sclerosis. Haemorrhages or blueberry muffin lesions may indicate a haematological condition, congenital infection or hypoxia. Bullae, pustules or scaling lesions may indicate a congenital infection such as varicella zoster or congenital syphilis, which includes the palms and soles, or dermatological conditions such as ichthyosis, and must be distinguished from maceration. If in doubt, take a skin biopsy specimen from a lesion. Meconium staining of the skin or orifices indicates intrauterine hypoxia.

Face

Cataracts may be present in congenital infections such as rubella^{33–35} and toxoplasmosis, as well as in systemic diseases, genetic conditions and inborn errors of metabolism. Hypertelorism with short palpebral fissures is part of the facial dysmorphism of fetal alcohol syndrome and fetal exposure to valproate. Low-set posteriorly rotated ears with flattened pinnae suggest anhydramnios due to renal disorder and Potter's sequence. Microtia and pre-auricular skin tags are frequent in Goldenhar syndrome. Creases of the ear lobe and pits on the undersurface are markers for Beckwith Weidemann syndrome. In otocephaly, both pinnae occur in the midline below the mouth, with congenital absence of the mandible. A short nose, a long smooth philtrum and a thin upper lip are seen in fetal alcohol syndrome and on exposure to valproate. A proboscis is frequent in trisomy 13 and may be situated above a midline cyclopic eye. Choanal atresia is found in CHARGE (coloboma, heart disease, atresia choanae, and retarded growth and development) syndrome. The CHD7 gene is mutated in 60% of postnatal cases.^{36–37}

Abnormal facial clefts may be seen in amniotic deformities, adhesions, mutilations (ADAM) syndrome. A visible tongue indicates the presence of macroglossia, as is seen in Beckwith Weidemann syndrome or with abnormalities of the CNS. An immobile tongue indicates a lack of swallowing and may be because of fetal akinesia. A tongue-tie may be present, which is associated with familial cleft lip and palate.

Micrognathia or retrognathia is often seen in aneuploidy. A horizontal crease on the chin may indicate renal disease.

Neck

The neck may show lateral skin webbing as is seen in monosomy X (XO) and multiple pterygium syndrome, or postnatal cystic hygroma, which occurs frequently in XO, trisomy 21 and trisomy 18. A posterior midline swelling could be due to a cervical meningocele. Fused cervical vertebrae raise the possibility of Klippel Feil syndrome. A groove around the neck with congestion of the face suggests strangulation by the umbilical cord.

Chest

A small abnormally shaped chest with short ribs is present in most skeletal dysplasias, which indicates pulmonary hypoplasia. A bell-shaped chest often indicates pulmonary hypoplasia, as may occur with anhydramnios. The chest may bulge asymmetrically, indicating a diaphragmatic hernia or pneumothorax. Palpable crepitus may occur following difficulty in ventilating the infant.

Abdomen

Abdominal distension can be due to ascites, organomegaly, gaseous distension of the bowel, intestinal obstruction and, rarely, a tumour. Defects of the body wall may be related to a short umbilical cord, a localised defect near the umbilicus as occurs in gastroschisis or failure of the bowel to return into the abdomen during development, as seen in an omphalocele.

Extremities

A simian crease and sandal gap typically occur in trisomy 21, polydactyly occurs in trisomy 13 and some skeletal dysplasias, and overgrowth of a digit occurs in Proteus syndrome. Syndactyly of the third and fourth digits is typical of triploidy and the placenta should be examined for partial molar change.

Genitalia

The external genitalia may be malformed or ambiguous, with associated renal and anal anomalies. Defects of the neural tube, pigmented lesions, abnormal tufts of hair and midline masses are frequent in the lumbar area.

Dissection

Standard neonatal textbooks explain the various dissection techniques.^{38–40}

The heart is dissected following the blood flow sequentially starting from the right atrium. Before dissection, the outflow tracts, aortic isthmus and ductus arteriosus are measured, and the measurements indicate the pattern of blood flow through the heart.⁴¹ Inflation and wax impregnation of the heart provide a permanent specimen,⁴² which is useful for teaching.

The brain-to-liver weight ratio is normally 2.5–3.5. Ratios of 5 and greater indicate asymmetric intrauterine growth retardation. The ratio of the combined weight of the lungs to the body weight is used to determine pulmonary hypoplasia. In infants below 28 weeks, a ratio of 0.015 or less indicates hypoplasia; above 28 weeks, the ratio for hypoplasia is 0.012 or less. Special dissection techniques are indicated if stenosis of the foramen magnum is suspected, as seen in

osteochondrodysplasia.⁴³ Rapid heat-accelerated fixation of the brain has recently been described.⁴⁴ The cerebral gyral pattern is compared with reference pictures that indicate when there is closure of the operculum and the development of gyri, culminating with three gyri in the temporal lobe at term. The transcerebellar diameter can be compared with reference values, and cerebellar microscopy, determining the presence of a lamina densicans, thickness of the outer granular layer and maturation of the Purkinje cells, all help in the assessment of maturation.^{45–46}

In the macerated infant measurements may be distorted, but the foot length remains a reliable estimate of gestational age.²⁷ Estimating the time of death includes macroscopic and microscopic criteria of the placenta and fetal organs.^{47–49} The costochondral junction may show interruption of growth. Careful dissection shows malformations. Asymmetric intrauterine growth retardation is often seen.

Placenta

The normal umbilical cord has one coil or twist per 5 cm. Hypercoiling of the umbilical cord indicates hypoxia.⁵⁰ Horizontal blocks of the maternal surface or squares of membrane may indicate maternal vascular disease.⁵¹ Cases with positive placental findings at perinatal autopsy range from 30% to 61%.^{52–57} Chorioamnionitis is the most common placental lesion associated with cerebral palsy in term and preterm infants.^{58–60} Fetal thrombotic vasculopathy may be present.^{61–62} Extensive placental infarction correlates with ischaemic cerebral injury, particularly periventricular white matter necrosis in stillbirths.⁶³

SPECIAL TECHNIQUES

A cytogenetic study of 136 cases showed an abnormal karyotype in 15.5% of stillbirths and in 25% of neonatal deaths.⁶⁴ All infants with an abnormal karyotype had congenital malformations. Time delays were crucial for obtaining positive cultures. A Dublin series of 75 unexplained stillbirths had an abnormal karyotype in 6 of 26 cases.⁶⁶

Fluorescent in situ hybridisation was performed on autopsy material to diagnose trisomy 18. A chromosome 18-specific centromere probe was used, and the test was positive in 9 of 10 cases. Macerated and archival tissues can be used for testing.⁶⁵

Fluorescent in situ hybridisation using liver cell touch preparations fixed in 95% ethanol is a low-cost and simplified method for diagnosing trisomies 21, 18 and 13 and monosomy X in autopsies of infants with congenital abnormalities.⁶⁶

PCR directed against the SRY gene has been used for rapid sex determination in patients with ambiguous genitalia.⁶⁷ Karyotyping is best reserved for patients with multiple congenital anomalies.^{68–69}

The Kleihauer–Betke test for fetomaternal haemorrhage was positive in 8% of a series of 75 unexplained stillbirths,⁶⁶ but a series of 745 stillbirths did not find it useful.⁵³ Fetal haemoglobin monoclonal antibodies in the maternal circulation can be detected by flow cytometry.⁷⁰ Differentiation of maternal and fetal erythrocytes in paraffin wax sections by using haemoglobin F immunostain with alkaline phosphatase as a substrate has been described.⁷¹

Raised levels of amniotic fluid erythropoietin indicate chronic fetal hypoxia in the uterus and may explain the cause of death in stillbirths. They correlate well with fetal erythropoietin levels.⁷²

DETECTION OF INFECTIOUS AGENTS

Common pathogens

Congenital infections (toxoplasma, rubella, cytomegalovirus and herpes simplex) and syphilis are screened for in early

pregnancy. In rare cases, perinatal deaths may be due to a congenital infection acquired during vaginal delivery. Changes in x ray, the presence of hydrops fetalis and organomegaly, particularly of the liver and spleen, may suggest the presence of congenital infection.

Detection of DNA sequences of herpes simplex virus by PCR in babies dying of neonatal herpes also localises the virus.⁷³ Herpes simplex virus isolated from an autopsy of the liver was serologically detected by immunofluorescence and confirmed by electron microscopy.⁷⁴

DNA, mRNA and early antigen for cytomegalovirus can be detected by immunocytochemistry, in situ hybridisation and in situ hybridisation—immunomax on autopsy of tissues. Early antigen was detected most often. DNA for cytomegalovirus was found more often than mRNA.⁷⁵

Most cases of syphilis have been treated in the uterus after maternal serology showed a positive result. Metaphysitis, marked splenomegaly, pericellular hepatic fibrosis and pulmonary fibrosis with extramedullary haemopoiesis are typical features. The diagnosis of congenital syphilis in severely macerated fetuses is facilitated by the examination of amniotic fluid by dark-field microscopy. Spirochaetes with the typical appearance and motility of *Treponema pallidum* are seen. Warthin Starry stain was positive in two of five cases and anti-treponema antibody immunofluorescence in one of three cases.⁷⁶

Toxoplasmosis causes hydrocephalus with intracerebral calcification.⁷⁷ PCR of amniotic fluid recognises the B1 gene of *Toxoplasma gondii* and can be completed in a day. A reported series provided an excellent detection rate, no false positives and one false negative test.⁷⁸ On autopsy *Toxoplasma* cysts may be seen in multiple tissues, ranging from the placenta to the brain. Testing for Rubella as a cause of death in stillbirths was not helpful.⁵³

Unusual pathogens

Coxsackie myocarditis is an uncommon cause of death in neonates. Coxsackie B3 antigens can be detected in formalin-fixed tissues by immunofluorescence on autopsy. In the myocardium, antigen is positive in both cardiac myocytes and endothelial cells. This observation was confirmed by electron microscopy.^{79–80} Recombinant Coxsackie enteroviral B3 capsid protein, VP1, was observed in necrotic cardiac myocytes and in islet cells of the pancreas by immunofluorescence.⁸¹ Adeno-associated virus antigen was detected by fluorescent antibody technique in infants dying from respiratory infections on autopsy.⁸² Viral antigens were detected by immunofluorescence in frozen or formalin-fixed specimens of lungs, kidneys, spleen, liver and lymph nodes on autopsy. The virus was confirmed by electron microscopy. Immunofluorescence provides a rapid diagnosis.⁸³

In southern Brazil, Chagas's disease is prevalent in pregnant women. Examination of the pericardial fluid from stillbirths by immunofluorescence for trypanosome proteins provides a reliable means of diagnosis. Complement fixation and haemagglutination can also be performed on the fluid.⁸⁴ *Trypanosoma cruzi* is rarely found in the placenta and infected infants may be negative for IgM antibodies.⁸⁵

IATROGENIC LESIONS

Prenatal maternal drug exposure may be due to therapeutic drugs—that is, warfarin for maternal prosthetic cardiac valves or deep vein thrombosis, and valproate for maternal epilepsy. Typical features of fetal Warfarin syndrome are a hypoplastic nose, stippled epiphyses or abnormality of the eye.⁸⁶ Spina bifida and craniofacial dysmorphism are also characteristic of fetal valproate syndrome.⁸⁷ Chorionic villus sampling, amniocentesis and cordocentesis carried out by experienced staff have a low risk of complication. In a series

of 873 intrapartum deaths from Trent, UK, 37 cases had traumatic deliveries. Cranial traumatic injury was always associated with physical difficulty at delivery and the use of instruments.⁸⁸⁻⁸⁹ Rare cases of spinal cord injury may occur.

Late complications of hyaline membrane disease include bronchopulmonary dysplasia. Complications of extracorporeal membrane oxygenation mainly include haemorrhage and sepsis.⁹⁰ Complications in neonatal intensive care may occur because of extreme prematurity⁹¹ or prolonged total parenteral nutrition.⁹² The death rates of infants from neonatal intensive care units have been declining.⁹³ A study of 75 infants from a neonatal intensive care unit from New Mexico examined the correlation between clinical diagnosis and autopsy. In 92% of cases the clinical diagnosis was confirmed. Agreement regarding the cause of death, however, was seen in only 50% of cases.⁹⁴

RISK FACTORS FOR PERINATAL INJURY

Premature infant

Maternal risk factors for preterm delivery include age <20 years, previous preterm birth, short interpregnancy interval, poor prenatal care, inadequate nutrition, low socioeconomic class, psychosocial stress, low prepregnancy weight, poor weight gain, short cervix, alcohol, cocaine, smoking, vaginal infections, urinary tract infections, sexually transmitted infections and sudden onset of pre-eclampsia.⁹⁵⁻¹⁰⁰ Probable placental lesions include the premature rupture of membranes, acute chorioamnionitis, placental ischaemia, chronic deciduitis, marginal separation with retroplacental haemorrhage, placenta praevia and marginal cord insertion.¹⁰¹⁻¹⁰² Causes of fetal death include fetal sepsis, abruption and fetal vascular thrombosis.

Small for gestational age or fetal growth restriction

Maternal risk factors include short stature, low weight, poor weight gain during pregnancy, smoking and abnormal uterine structure, pre-eclampsia, thrombophilia and renovascular disease, reproductive failure, and autoimmunity.¹⁰³⁻¹⁰⁹

Take-home messages

- Pre-autopsy checklist should include consent, x ray, correlation with ultrasound, and photography. Special cases may need magnetic resonance imaging or metabolic tests.
- Morphometry and careful examination, paying attention to head and skull, skin, face, neck, chest, abdomen, extremities and genitalia, followed by dissection of the fetus and placenta, should permit the pathologist to classify the fetus. Categories include normal macerated, hydropic, congenital anomaly or fresh normal, as well as small, appropriate and large gestational age. Foot length is most reliable in the macerated fetus.
- Special techniques may be required to make a definitive diagnosis, such as cytogenetics by fluorescent in situ hybridisation, and immunofluorescence for common and unusual infectious agents.
- Determine what risk factors, in utero, during delivery or postnatally, may have contributed to the adverse fetal outcome. Timing of death by assessing the degree of maceration may help in interpretation of the case.
- Ensure that the final report answers the questions that were posed by the clinicians and provides information for counselling for a future pregnancy.

Fetal causes represent genetic and chromosomal disorders, including confined placental mosaicism. Placental lesions include chronic abruption, chronic villitis, fetal thrombotic vasculopathy, chronic intervillitis and massive perivillous fibrin deposition.¹⁰³⁻¹¹⁰⁻¹¹¹ Clinically reduced Doppler flow, followed by reversed Doppler flow, followed by intrauterine death occurs unless there is intervention.¹¹²⁻¹¹³ Causes of death include atherosclerosis of maternal vessels and malformations in the fetus if aneuploidy is present.

Hypoxic-ischaemic injury or birth asphyxia

Maternal factors include thyroid disease, vaginal bleeding during pregnancy, postdated pregnancy, diabetes, renal disease, essential hypertension, malnutrition and anaemia.¹¹⁴⁻¹¹⁷ Fetal factors include thrombophilia, being large for gestational age and incomplete flexion of the head.⁶²⁻¹¹⁸⁻¹²² Placental lesions that cause circulatory disruption include uteroplacental separation, fetal haemorrhage, umbilical cord compression, placental thromboemboli and placenta praevia. Both villous oedema and infarction impair placental exchange. Placental lesions known to be associated with subsequent neurological impairment include avascular villi, haemosiderin in the chorionic plate, fetal vascular thrombosis and severe inflammation.¹²¹⁻¹²³⁻¹²⁷ Fetal lesions depend on gestational age, and the nature and duration of the insult. Preterm infants develop necrosis of white matter and gliosis. In term infants the predominant site of injury is the central grey matter, although lesions of white matter may also occur.¹²⁸

Hydrops fetalis

Hydrops indicates the presence of heart failure, anaemia or hypoproteinaemia, or a combination.¹²⁹ It is often non-immune. Cardiovascular causes include structural defects and arrhythmias, and account for 22% of cases. Pulmonary and thoracic lesions account for 16%, anaemias for 12% and chromosomal abnormalities for 10% of cases. Minor lesions include fetal infections, malformations of the urinary tract, tumours, storage diseases and metabolic causes. In all, 19% of cases remain undetermined after a complete autopsy.¹³⁰

TIMING OF INSULTS

Placenta

Placental lesions may be chronic, subacute or acute. Villous intravascular karyorrhexis occurs 6 h after death, with septation of stem villous vessels by 2 days. If extensive, death occurred 2 weeks previously.⁴⁷ Meconium is present in chorionic macrophages after 3 h.¹³¹ Meconium is often associated with chorioamnionitis and fetal thrombotic vasculopathy, which result in severe morbidity.¹³² A recent study has shown enhanced growth of group B *Streptococcus* in the presence of meconium.¹³³

Fetus

The degree of skin loss in maceration allows us to estimate the time of death. A skin loss of size 1 cm indicates 6 h and mummification 2 weeks after death.⁴⁸ Microscopic examination for loss of nuclear basophilia in various tissues provides an estimate of the time of death.⁴⁹ Adrenal fat distribution indicates whether the mode of death was acute or chronic.¹³⁴ The costochondral junction may indicate growth arrest.¹³⁵⁻¹³⁶ The microscopic appearance of the thymus indicates the duration of illness. Mineralisation of necrotic neurones, vascular proliferation, gitter cells and cyst formation help in determining the duration of cerebral necrosis.¹³⁷⁻¹³⁸

CONCLUSION

The role of perinatal autopsy is to provide answers to parents and clinicians regarding the cause of death and congenital anomalies. It also provides an audit of ultrasonographic

diagnosis, obstetric and neonatal intensive care.¹³⁹ The cost of autopsy has a role in the diagnosis:¹⁴⁰ it is vital for teaching, training, research and epidemiology. If perinatal autopsy fails to fulfil these requirements, it will be replaced by imaging techniques, needle biopsies and verbal autopsy.^{141–146} In cases of fetal malformation, only a complete autopsy will detect all abnormalities, which may be crucial in providing appropriate counselling to the family for a subsequent pregnancy.^{147–148}

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ECHO

More endoscopists improve outcome for upper GI cancer

Please visit the *Quality and Safety in Health Care* website [www.qshc.com] for a link to the full text of this article.

More endoscopists may be the answer to better outcomes for upper gastrointestinal (GI) cancer, as recent improvement seems to owe more to the introduction of nurse endoscopists than the UK government's two week wait scheme for a specialist consultation, according to doctors in one cancer unit.

True enough, the odds of curative resection increased significantly (odds ratio 1.48) in their unit in the two years after the scheme was introduced compared with the two years before, and curative resections for early (stage 1 and 2) cancers rose from 47 to 58. But only two patients (5%) of 38 diagnosed with the cancer out of 623 referred under the scheme had early stage disease compared with 56 (27%) outside it. Furthermore, just over a third of patients with early stage cancer had symptoms consistent with the referral criteria in the scheme, but only two of them were referred under it.

When the scheme was implemented at Norfolk and Norwich University Hospital, in September 2000, it coincided with appointment of two full time nurse endoscopists, which reduced routine waiting times for endoscopy—and probably accounted for the improvement.

Under the scheme guidelines for urgent referrals for upper GI cancer were issued to general practitioners to ensure timely specialist evaluation. Detecting the cancer early is key to curative treatment, but symptoms can be unreliable. This may be why reducing times for routine endoscopy may be the best option.

The UK government has been under pressure to improve its poor record on upper GI cancer outcome in western Europe.

▲ Spahos T, *et al*. *Postgraduate Medical Journal* 2005;**81**:723–730.