ROYAL COLLEGE OF
OBSTETRICIANS AND GYNAECOLOGISTS
AND
ROYAL COLLEGE OF PATHOLOGISTS

Fetal and Perinatal Pathology

Report of a Joint Working Party

Setting standards to improve women's health
June 2001

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CONTENTS PAGE

THE WORKING PARTY

Professor Nicholas Fisk FRCOG (Chairman)
Professor of Obstetrics and Gynaecology, Imperial College School of Medicine, Queen Charlotte's and Chelsea Hospital, London.

Professor P Jem Berry FRCPath
Professor of Paediatric Pathology, University of Bristol, St Michael's Hospital, Bristol.

Dr Iona Jeffrey FRCPath
Consultant Perinatal Pathologist, St George's Hospital, London.

Dr Mary Macintosh MRCOG
Director, Confidential Enquiries into Stillbirths and Deaths in Infancy.

Mr Stephen Walkinshaw MRCOG
Consultant in Maternal and Fetal Medicine, Liverpool Women's Hospital, Liverpool.

The following member was co-opted to represent The Royal College of Paediatrics and Child Health:

Dr Sunil Sinha FRCPCH
Consultant Neonatologist, South Cleveland Maternity Hospital, Middlesborough.

Administrative Support:

Ms Alison Gawith
Committee Secretary, Royal College of Obstetricians and Gynaecologists

We acknowledge with thanks advice from the following:

Ms Maggie Fitchett
Chairman, Association of Clinical Cytogeneticists.

FOREWORD

This report has been produced jointly by the Royal College of Obstetricians and Gynaecologists and the Royal College of Pathology. It updates the previous document issued by the two Colleges in 1988. Clearly, some 12 years on, there have been major changes in issues of importance regarding fetal and perinatal pathology. Many of these have been highlighted in recent Confidential Enquiries into Stillbirths and Deaths in Infancy. A number of the tests suggested by the 1988 report have been superseded by more appropriate investigations, while new ones have been developed that give greater insight into the causes of fetal and neonatal death. Not only have consumer expectations increased greatly but the last decade has also seen the emergence of the subspecialty of fetal and maternal medicine, the advent of information technology and organisational changes in the provision of specialist pathology services. These recommendations should ensure high-quality perinatal pathology services in keeping with recent scientific advances and modern standards of patient consent.

RECOMMENDATIONS

1. Subspecialty service provision (Section 2)

The Working Party considers the arguments for full regionalisation and subspecialisation of perinatal pathology services to be overwhelming. The Royal College of Pathologists and the Royal College of Obstetricians and Gynaecologists should together support the principle of national implementation of subspecialist perinatal pathology services. The organisation of specialist perinatal pathology service-provision should be reviewed and improved. This will require new service specifications, manpower planning, resource allocation and alterations to the training of perinatal pathologists.

2. Implementation (Section 2)

To optimise the efficiency of existing services, it is recommended that regional specialist commissioning groups make perinatal pathology a priority to ensure that adequately funded, auditable and accountable services are in place. Full specialisation will require the creation of 40–50% more consultant posts in perinatal pathology.

3. Local service provision (Section 2)

The Working Party considers that local provision of perinatal pathology services by general histopathologists who have no special interest or training is no longer appropriate.

4. Transitional arrangements (Section 2)

Subspecialisation will take time to implement. In the interim, any trust providing a clinical service in obstetrics and/or fetal medicine and not referring all postmortem examinations to a tertiary perinatal pathology unit should have an identified lead pathologist with responsibility for:

(i) implementing protocols agreed with the tertiary centre
(ii) establishing agreed local guidelines for the referral of complex cases
(iii) attending local perinatal mortality meetings
(iv) auditing the quality of postmortem examinations carried out locally
(v) participating in appropriate continuing professional development.

The minimum annual workload for a lead local pathologist is 50 perinatal cases per year.

5. Training of pathologists (Section 3)

The training programme and examination structure in fetal, perinatal and paediatric pathology should be reviewed to ensure that:

(i) sufficient training posts are provided at recognised centres for the training of specialist perinatal/paediatric pathologists to meet current demands and future expansion as described above
(ii) general histopathologists have an adequate grounding in fetal and perinatal pathology for as long as general histopathologists undertake perinatal work as part of the transitional arrangements described above.

The Working Party considers that the only effective way of increasing the status of paediatric and perinatal pathology and streamlining paediatric and perinatal pathology training schemes would be for paediatric and perinatal

pathology to be recognised as a full subspecialty with its own protected training numbers.

6. Training of obstetricians (Section 3)

It is recommended that the training syllabus be amended to require obstetricians in training to attend perinatal autopsies.

7. Minimum standards for perinatal autopsy (Section 3)

The Working Party has revised and updated the 1993 minimum standards for perinatal pathology. The revised minimum standards are given in Appendix 1.

8. Termination for fetal abnormality (Section 4)

Non-surgical methods should be employed for terminations for fetal structural abnormalities, to allow pathological examination. The only exceptions should be terminations for known aneuploidy or those before 11 weeks of gestation, where the surgical technique can be modified to deliver an intact specimen.

9. Limited autopsy (Section 4)

Parents who decline perinatal autopsy should be offered limited autopsy. Clinically useful information may still be obtained from external examination, tissue biopsy, body-cavity aspiration and imaging.

10. Cytogenetics (Section 4)

Because of the high failure rate of post-abortal and post-stillbirth karyotyping, the Working Party recommends that multiple samples be collected, usually placenta and full- thickness skin. Consideration should also be given to collecting a specimen in utero before the termination process begins.

11. DNA studies (Section 4)

As an increasing number of malformations are shown to have a genetic basis, it is recommended that fetal tissue and/or DNA be stored for subsequent molecular testing from all euploid fetuses with more than one malformation. Molecular tests are already available for a range of conditions that might be identified at perinatal autopsy, including the CATCH phenotype, myotonic dystrophy, thanatophoric dwarfism, Miller–Diecker syndrome, spinal muscular atrophy and medium chain acyl CoA dehydrogenase deficiency.

12. Placental pathology (Section 5)

In addition to existing indications (small-for-gestational-age, very-low-birthweight and multiple pregnancy), the placenta should be examined in cases of neonatal hypoxic ischaemic encephalopathy, preterm labour at less than 34 weeks of gestation, congenital malformations, macroscopic placental abnormalities, recurrent antepartum haemorrhage, clinical chorioamnionitis, maternal diabetes and severe pre-eclampsia.

13. Consent to autopsy (Section 6)

The Working Party supports the recent CESDI guidance on procedures for obtaining consent. Targets for autopsy rates are no longer considered

appropriate and, instead, the quality of the offer of autopsy could be audited. Although there is no legal requirement, there is an ethical requirement and consent should now be sought for all examinations of all fetal specimens of less than 24 weeks of gestation. In some circumstances, it is good practice to retain organs, such as the heart or brain, for later detailed examination. Specific consent for organ retention is essential.

14. Consent for research (Section 6)

The 1988 Polkinghorne guidelines on the use of fetal material in research need revision to bring them into line with modern standards of consent and to take account of recent research developments in fetal medicine.

15. Information technology (Section 7)

Information technology will have particular application in fetal and perinatal pathology, by linking pathologists to databases and by facilitating information transfer of images and reports. To encourage compliance with minimal standards and to facilitate audit, the Working Party recommends that standard perinatal autopsy request and report forms be made available for downloading from the internet.

1 INTRODUCTION

1.1 Definition

For the purposes of this report, fetal and perinatal pathology is taken to include embryonic, fetal, perinatal and neonatal pathology. The term 'perinatal pathology' embraces all the above terms.

1.2 The first report

The first joint report from the Royal College of Obstetricians and Gynaecologists and the Royal College of Pathologists Working Party was published in 1988.[1] The report:

- suggested establishing minimum requirements for perinatal autopsy for examination of mid-trimester abortuses and for placental examination
- recommended that consent to perinatal autopsy be encouraged and that autopsy rates of less than 75% were unacceptable
- laid down guidelines for external and radiological examination and for maternal and fetal/neonatal laboratory investigations in cases of perinatal death
- recommended that placentas be examined from all stillbirths, multiple pregnancies, low birthweight and small-for-gestational age babies and abnormal pregnancies
- recommended the institution of regional enquiries into perinatal mortality
- advocated the establishment of regional perinatal pathology services, together with the formation of regional units in some regions.

1.3 Factors contributing to need for a second report

1.3.1 Autopsy rates

Although autopsy rates may appear to have improved from below 50% in some regions to as high as 66–69% in published regional audits,[2–5] national rates have actually fallen. Data from England, Wales and Northern Ireland reported to the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI)[6] show a decline since 1994 from 59% to 54%. Understandably, rates are higher for stillbirths than neonatal deaths (62% versus 41% in 1997), although the highest regional rate for stillbirths still falls short of the 75% minimum recommended in the first report. In at least 15% of cases where there was no autopsy, one had not been requested by the relevant clinician.

1.3.2 Quality of autopsy

There is concern that negative professional perceptions of the value of perinatal autopsy have adversely influenced autopsy rates.[5,7–10] In 1993, the Royal College of Pathologists and the National Advisory Board to CESDI issued minimum guidelines for perinatal autopsies.[8] However, in the Northern Region in 1994, only 51% of necropsies met these standards and the placenta was examined in only 24% of early neonatal deaths.[8] The quality of perinatal autopsy appears to have improved since then. In Wales, only 54% of autopsies complied with the minimum standard in 1993 but rose to 93% in

1996.[3] CESDI audits by specialist perinatal pathologists show that the rate of autopsy reports deemed 'poor' fell from 47% in 1994 to 39% in 1995.[6] Notwithstanding this, histology was considered inadequate in 50% of cases and the interpretative summary or commentary inadequate in 57%. The probability of a perinatal autopsy providing clinically significant information has been directly related to the quality of the report, as assessed by its detail and the number of ancillary investigations undertaken.[4]

1.3.3 Changing expectations

The trend to lower family size and older maternal age at childbearing, together with the rarity of perinatal death (around eight in 1000) has led to increased parental expectations that every pregnancy will have a normal outcome. Such views are fuelled by technological advances. Most fetuses are now screened for aneuploidy, structural anomalies and fetal wellbeing, while the results of neonatal intensive care and fetal therapy are given prominence in the media. Parents may also be better informed from medical information widely available on the internet. The understandable insistence of many parents on full explanations when things go wrong has obvious parallels in obstetric risk management and litigation. Similarly, standards of consent have increased, in part in response to public expectations. This is indicated in the emotive area of paediatric and perinatal autopsy by the recent public outcry over whole-organ retention.[11]

1.3.4 Medical advances

The last decade has seen the establishment of tertiary-referral fetal medicine centres in most regions. This subspecialty of fetal and maternal medicine arose as a result of the now widespread availability of high-resolution ultrasound, the diagnostic and therapeutic access to the fetus provided by invasive procedures and advances in laboratory technology. At district level, the rate of major anomaly detection (1–2% of pregnancies in the best centres[12,13]) continues to improve, while the increase in nuchal translucency screening creates additional demands for pathology on early fetal specimens.[14] The explosion in molecular knowledge has led to identification of over one thousand single-gene disorders, including those with non-Mendelian effects on the fetus, such as myotonic dystrophy, hereditary thrombophilias and genes influencing fetal growth. The imminent completion of the Human Genome Mapping Project, together with its derivative field of proteomics, is set to determine the basis of many multifactorial obstetric and fetal pathologies (for example, neural-tube defects and pre-eclampsia). Storage of fetal DNA at perinatal autopsy now assumes considerable importance.

1.3.5 Changing role of perinatal pathology

Two major areas of workload in perinatal pathology, as an autopsy-based specialty, are stillbirths and congenital anomalies. Unexplained antepartum stillbirth is now the leading cause of stillbirth (3.8 in 1000) and accounts for almost twice as many deaths as prematurity and six times as many as sudden infant death syndrome.[10] The role of a rigorous autopsy lies in excluding known causes of death as well as identifying predisposing factors (such as suboptimal growth or placental villitis). After termination of pregnancy for ultrasonically diagnosed congenital anomalies, it is well established that

important additional information is obtained in 20–40% of cases, in many of which the risk of recurrence is altered as a result.[15–19] This now applies throughout pregnancy, following the removal of any gestational limit to termination for serious fetal abnormality in the modifications to this clause under the Human Fertilisation and Embryology Act 1990 (Clause E: Substantial risk of serious mental or physical handicap).

1.3.6 Service development

Although there is now a perinatal pathologist in every region and most fetal medicine services have established links with a perinatal pathologist, developments in fetal medicine have not been matched by parallel developments in the provision of perinatal pathology services. Much perinatal pathology is still performed in large parts of the country by general histopathologists. Autopsies performed by specialist perinatal pathologists in regional centres are more likely than those completed in non-regional centres to conform to minimum standards (92–100 versus 28–69%) and to yield additional information.[3,4] The Clothier report[20] recommended specialist paediatric pathology in all cases of unexpected or clinically unaccountable death in children. In 1995, the Royal College of Pathologists issued service specifications for purchasers of perinatal histopathology.[21] These strongly encouraged the development of regional centres in perinatal pathology but considered that the ideal of all perinatal postmortem examinations being carried out by someone with specialist knowledge was unrealistic at that time. There seems little doubt that the CESDI audits have encouraged referrals to regional centres. The trend towards subspecialisation is supported by both Colleges and there are few arguments against it other than logistics.[9]

1.3.7 Low status of perinatal pathology

Fetal and perinatal pathology is a shortage specialty. Recruitment is often difficult in small specialities but it seems to be exacerbated in perinatal pathology by several factors:

- Remuneration is poor relative to general histopathology, with little scope for private or coroner's work.
- Although perinatal pathology is *de facto* recognised as a subspecialty of histopathology, it does not have its own Certificate of Completion of Specialist Training (CCST).
- There is limited exposure to perinatal pathology during general histopathological training, while trainees with experience in a related clinical discipline are still required to undertake training in adult histopathology.
- Perinatal pathology is perceived as the least attractive of the special interest areas in histopathology.
- Working conditions for many consultants are poor and they often work single-handed, with limited support staff and no identifiable budget.[22]

2 SERVICE

In practice, a perinatal pathology service covers embryonic, fetal, perinatal, neonatal and infant pathology. The relevant specialisation within histopathology has been known as paediatric and perinatal pathology. Around 90% of specialist paediatric and perinatal pathologists in the UK do perinatal work. This report concentrates on fetal and perinatal service provision. Its recommendations are intended to optimise existing opportunities for service provision and to ensure an adequate supply of newly trained perinatal and paediatric pathologists in the future.

2.1 Models of service provision

The pattern of provision of fetal and perinatal pathology has varied depending on historical and geographical factors. There are three service models:

- complete regionalisation in subspecialty centres
- local provision by general histopathologists
- hub-and-spoke networks focused on a subspecialty centre with local services provided by lead general pathologists with a perinatal interest.

A chief issue is the desirability and practicability of full subspecialty service provision.

2.2 Subspecialty service

2.2.1 Rationale for specialist departments of perinatal pathology

The following passage is taken from the Royal College of Pathologists Service Specification.[21]

> 'Perinatal pathology requires knowledge of obstetrics, paediatrics genetics, syndromology and diseases of the newborn, usually acquired during a period of prolonged training over and above that undertaken by general pathologists. Expertise in perinatal pathology is sustained by regular contact with specialists in the corresponding clinical disciplines. An important feature of perinatal postmortems is the meticulous documentation of abnormality and normality by photography, radiology, cytogenetics and other laboratory tests and discussion of findings with colleagues in clinical genetics, microbiology, clinical chemistry, paediatric haematology and paediatric radiology. Interpretation requires access to specialist books, journals and computer databases. These resources are seldom available in district general hospitals. For this reason and to make the best use of scarce resources, perinatal necropsies are best carried out in regional centres.'

2.2.2 Clinical need

The poor quality of perinatal autopsies has been constantly highlighted by CESDI, which was set up in response to the first joint Working Party report.[1] The House of Commons Health Committee report of 1992 observed that 'we do not see how the Government's initiative to find out why particular babies

die can be carried out unless a proper service (for perinatal pathology) is in place'.[23] A few regional posts were set up in response to CESDI's requirements. There is now some evidence that the quality of perinatal autopsies is improving, albeit slightly (see section 1.2.6).[6] More referrals are being made to regional centres, which improves quality.[3] Consistently high-quality perinatal autopsy reports seem confined to subspecialty centres[3] and quality autopsies are more likely to reveal the cause of death or additional clinically important information.[4] This trend towards subspecialisation is supported by CESDI, by the Clothier report, by both the Royal College of Pathologists and the Royal College of Obstetricians and Gynaecologists and by most specialist perinatal pathologists[6,8,9,21,24] Clinical governance should be a further stimulus to subspecialisation.

2.2.3 Facilities

The 1995 service specification requires two consultant pathologists for a specialist paediatric and perinatal pathology department.[21] Appropriate facilities are listed as:

- adequate secretarial support and communications
- dedicated mortuary space
- access to radiology and photography for all cases
- access to cytogenetics and clinical genetics or at least to a clinical genetics database
- ultra-low-temperature freezer for storage of samples including DNA
- adequate viewing room or chapel
- proper arrangements for disposal of fetuses
- specialist textbooks and journals.

Specialist departments are required to participate in external quality assurance and research and development.

2.2.4 Disadvantages

One disadvantage is that autopsies are performed away from the local hospital. This goes against the established principle that autopsies (in adults) should be performed in the local hospital to enable the clinicians to attend and contribute to the interpretation of findings. The considerable arguments for regionalisation for quality and facilities overcome this objection. As autopsies take only a few hours, bodies can be returned relatively swiftly to the hospital in which the baby died. The service specification has recommended that, in order to compensate for not performing the autopsy in the local hospital, regional departments must provide excellent communication and regional perinatal pathologists must be enabled to attend local mortality and audit meetings and to take part in local postgraduate activities.[21] Another potential disadvantage is the deskilling of general histopathologists, although this becomes less relevant if perinatal services are exclusively provided by perinatal pathologists.

2.2.5 Manpower

It had been estimated earlier that each regional centre staffed by two paediatric/perinatal pathologists should be sufficient to meet the needs of a

population of three million.[21] Regions with large children's hospitals or major fetal medicine centres would clearly need more. At the same time, an adequate workload for a perinatal pathology department to maintain expertise was estimated at '100 paediatric postmortems and/or 100 fetal examinations'.[21] A recent survey from the Royal College of Pathologists suggested that the average workload for a perinatal pathologist was equivalent to 200 autopsies and 500 placental examinations annually.[22] Although precise workload figures are not available, the current national load of relevant examinations can be estimated. CESDI data for 1997 indicate that 54.5% of 10418 deaths after 20 weeks underwent autopsy (= 5667 cases).[6] Regional data from the North West Thames Region over the last five years indicate that 30% of referrals are from fetuses before 20 weeks (+1700 = 7367 cases/year).[25] Correcting this figure for Scottish data not included in CESDI leads to an estimated UK annual workload of 8045 cases. This figure takes no account of the likely effect on autopsy rates of improved quality from specialisation of perinatal pathology services. Based on the Royal College of Pathologists' service specifications for perinatal pathology,[21] this figure represents an average workload for 40 full-time perinatal pathologists. Given that around 40% of perinatal pathologists are academics contracted for 6/11 clinical sessions,[22] 46 perinatal pathologists would be required to cover the estimated current national workload. This figure makes no allowance for non-perinatal paediatric pathology.

2.3 Local service

2.3.1 Rationale

The primary rationale for this service has been logistic, i.e. the paucity of specialist perinatal pathology centres.[8,9] The Royal College of Pathologists' 1995 guidance[21] for purchasers of perinatal pathology services contrasted the ideal of subspecialty service provision with the practicality that 'the number of these examinations makes this unrealistic'.

2.3.2 Current practice

Although there is evidence from some regions that the majority of perinatal pathology services are now provided in specialist units,[3] the extent of local service provision nationally has not been quantified. Historically, individual histopathologists in some areas developed a special interest in perinatal pathology, providing a valuable interim service as lead pathologist. Empirically, however, much routine work appears still to be carried out by district general histopathologists, who deal with many of the cases listed in Section 2.2.5 above.

2.3.3 The future

It is difficult to see how quality can be improved within the context of a busy general workload, especially against the background of the increasing complexity of perinatal pathology, increased parental expectations and modern audit requirements. The low priority attached to perinatal pathology as a discipline within histopathology is a further disincentive to maintaining this model. The Working Party considers that local provision of perinatal pathology services by general histopathologists is no longer acceptable.

2.4 Barriers to subspecialisation

2.4.1 Status

Forensic pathology and neuropathology are recognised subspecialties of histopathology but paediatric and perinatal pathology is not. This distinction is important, in that it is widely recognised that neuropathology is outwith the remit of general histopathologists, whereas fetal and perinatal pathology is not. The other criteria for a subspecialty, that of specialised techniques, applies similarly to both.

2.4.2 Manpower

In a 1999 survey,[22] there were 42 paediatric and perinatal pathologists in the UK, of whom approximately six do no perinatal work. Allowing for non-perinatal paediatric pathology and the sessional commitments of academics, it can be estimated that an additional 14 perinatal pathologists would be needed to deal with the current national workload. These could be accommodated in the existing number of departments (= 23), which would end the single-consultant service currently provided by one in four perinatal pathology services.[22]

2.4.3 Resource implications

There is little point in increasing or redirecting consultant manpower unless the additional infrastructure facilities addressed in Section 2.2.3 are resourced.

2.5 Implementation of subspecialisation

2.5.1 Principle

The Working Party considers the arguments for regionalisation/subspecialisation of perinatal pathology services to be overwhelming. The Royal College of Pathologists and the Royal College of Obstetricians and Gynaecologists should together support the principle of national implementation of subspecialist perinatal pathology services. Further endorsement could be sought from the Royal College of Paediatrics and Child Health. The organisation of specialist perinatal pathology service provision should be reviewed and improved. This will require revised service specifications, manpower planning and resource allocation.

2.5.2 Logistics

Complete subspecialisation could be provided either through regional centres (old health regions), although in many centres there would need to be more than two specialist perinatal pathologists to cope with the workload. An alternative would be to retain the model of two specialist perinatal pathologists per perinatal pathology centre but spread them more widely according to workload, with many regions having more than one centre. This could be decided on the basis of local geography in relation to providers of fetal medicine and neonatal intensive care services. Given the importance of maintaining contacts with local obstetric hospitals through feedback and perinatal morbidity meetings, a larger number of units staffed with two perinatal pathologists would seem to be preferable. The current number of

centres undertaking perinatal pathology (= 23) is an adequate framework for the universal provision of subspecialist services.

2.5.3 Cost

Although the costs of implementation are outside the remit of this report, it is noted that the additional resource implications are minor compared with the recent drive towards an around-the-clock consultant-based labour-ward service.

2.6 Transitional arrangements

2.6.1 Philosophy

Accepting that the above moves will take time, the priority in the interim is to achieve higher standards of fetal and perinatal pathology. This is only likely to be achieved in many areas through improving services in large district general hospitals. In other regions, local perinatal pathologists could do much more if they had proper regional funding.

2.6.2 Existing departments of perinatal and paediatric pathology

These are often underfunded and understaffed. It is recommended that regional specialist commissioning groups make perinatal pathology a priority in order to ensure that adequately funded, auditable and accountable services are in place and to optimise the efficiency of existing services.

2.6.3 Local service provision

Any trust that provides a clinical service in obstetrics and does not refer all postmortems to a tertiary perinatal pathology unit should have an identified lead pathologist with responsibility for:

- implementing protocols agreed with the tertiary centre (hub-and-spoke model)
- establishing agreed local guidelines for the referral of complex cases
- attending local perinatal mortality meetings
- auditing the quality of postmortem examinations carried out locally
- participating in appropriate continuing professional development, which might include a period in the local specialist perinatal pathology centre.

2.6.4 Quality assurance

The minimum adequate workload for a lead pathologist in these circumstances is 50 cases per year. This should be audited. There is already an External Quality Assurance Scheme for tertiary paediatric pathologists run by the British Paediatric Pathology Association. The Working Party recommends that participation in a similar scheme for pathologists 'with an interest' should be a criterion for providing the service locally.

3 RECRUITMENT AND TRAINING

3.1 Recruitment of specialist pathologists

3.1.1 Shortage

Fetal and perinatal pathology is a shortage specialty and, unless major steps are taken, it is likely to remain so for the foreseeable future. A recent survey showed that there were six consultant posts vacant, with 14 retirements expected in the next ten years. There are currently only three trainees in post, with a further two training posts vacant. At least four training posts in perinatal and paediatric pathology have been lost since the early 1990s, either converted into consultant posts or subsumed into general histopathology training schemes following the implementation of the Calman report.

3.1.2 Additional training posts

Manpower planning in paediatric and perinatal pathology needs to be reviewed in order to determine the numbers of trainees required to achieve full subspecialisation and to allow such training to be provided within the constraints of current departments. Even without expanding the service, the current number of trainees is insufficient to meet existing vacancies and future retirements. Action will be needed to remedy from postgraduate deans and the Specialist Workforce Advisory Group. It will require protected training numbers for the subspecialty as well as funding by NHS trusts.

3.1.3 Recruiting trainees

The Royal College of Pathologists' training syllabus urges that 'consideration be given to methods to attract trainees into paediatric pathology, since there are still too few candidates of sufficient standard to meet demands. Too often, the field for a paediatric job is of lower standard than a similar general histopathology appointment in the same unit'. The Working Party supports moves to encourage recruitment into the subspecialty. In particular, it is important that any disincentives to potential specialist perinatal and paediatric pathologists are removed from the College's training system.

3.1.4 Entry

The 40% expansion in consultant appointments required for implementation of full subspecialty service provision necessarily involves attracting far greater numbers into the specialty than previously. However, vacancies in the current low numbers of training posts indicate that the problem is far broader than that of training-post availability. Pathology trainees tend to view paediatric and perinatal pathology as an unattractive branch of pathology, involving predominantly autopsy rather than more sophisticated investigations and associated with low status and remuneration. Further, many trainees seem to go into general histopathology so that they can maintain a general overview of specialties.

3.1.5 Suggestions

Addressing the adequacy of working conditions of specialist fetal and perinatal pathologists within the move to full subspecialisation should go some way to improve recruitment. Another solution would be to expose students at

undergraduate level. Recruitment should be encouraged at SHO level, not just from a pathology background but also from relevant clinical backgrounds. The attractive features of perinatal pathology are molecular advances in the understanding of disease, the enormous research opportunities, the fact that it is an academic discipline and the close interaction with clinicians in fetal medicine, obstetrics and neonatology. These features could be emphasised to general pathology trainees in their first two years.

3.2 Training of specialist pathologists

3.2.1 Current RCPath training

The Royal College of Pathologists currently recommends four years in higher specialist training in histopathology. In year two, a minimum of four weeks is spent doing perinatal and paediatric pathology, in which a minimum of five supervised fetal and perinatal autopsies should be performed. It is recommended that trainees have an approach to malformation syndromes, are able to recognise non-accidental injury and to tackle congenital heart disease, and are able to examine a placenta and recognise common lesions. They should have attended at least one perinatal mortality meeting. During years three and four, a minimum of a further month is spent in paediatric and perinatal pathology. Thus, most pathologists taking up their first consultant post will have had only limited exposure (i.e. two months) to perinatal pathology.

3.2.2 Current perinatal pathology training

For specialist training in paediatric pathology, the recommendation is currently that a minimum of two years are spent in designated departments of perinatal and paediatric pathology, following a good grounding in general histopathology. Currently, this option is available in years three and four of higher specialist training. The Royal College of Pathologists' training programme has recently been reviewed.[26] Training can now be slanted towards a subspecialty in the first two years, with the Part 2 examination entirely devoted to subspecialty practice.

3.2.3 General proposals

The training programme and examination structure in fetal, perinatal and paediatric pathology should be reviewed regularly to ensure that:

(a) adequate posts at recognised centres are provided for the training of sufficient specialist perinatal and paediatric pathologists to meet current demands and future expansion as described in Sections 2.4.2 and 2.5.2.

(b) general histopathologists have an adequate grounding in fetal and perinatal pathology for as long as general histopathologists undertake perinatal work as part of the transitional arrangements described in Section 3.6.

3.2.4 Diploma

The Working Party considered the option of a Diploma in Paediatric and Perinatal Pathology to acknowledge special-interest training short of subspecialty training, as might be suitable for lead clinicians with an

interest. This was rejected, as improved training for generalists is only a transitional issue and the priority instead lies in facilitating and implementing training in pursuit of full subspecialty service provision.

3.2.5 Full recognition as a subspecialty

The Working Party considered that the only effective way of increasing the status of paediatric and perinatal pathology and streamlining paediatric and perinatal pathology training schemes would be for paediatric and perinatal pathology to be recognised as a full subspecialty with its own protected training numbers.

3.3 Training of specialist obstetricians

3.3.1 Need for greater exposure

As discussed above, there is evidence that some obstetricians have low expectations of a perinatal autopsy and negative perceptions of its role. This adversely affects autopsy rates, through obstetricians either not informing parents of the potentially beneficial information that may result from a perinatal autopsy or, in some cases, not even requesting one. This could relatively easily be addressed through the specialist training programme. The importance of training in the obtaining of consent is also stressed.

3.3.2 Current specialist training

The syllabus requires trainees 'to manage perinatal death' (Module 8B, Target 17 of log book). This incorporates a short counselling course and attendance at a perinatal meeting. There is no requirement to attend a perinatal autopsy.

3.3.3 Exposure to perinatal autopsy

The Working Party considered it advantageous for trainees to attend at least one perinatal autopsy. Observing perinatal autopsies would give better understanding of the information elicited during an autopsy and the importance of appropriate clinical information. In particular, obstetricians in training would observe the considerable technical skill taken with intracranial and other organ inspection and sampling and reconstruction to minimise disfigurement and preserve the external appearance of the baby. Indeed, it is difficult to envisage how clinicians in obstetrics or neonatology can obtain informed consent without having been exposed to a perinatal autopsy. In addition to autopsy attendance, perinatal pathology should figure as one of the topics addressed during formal Calman teaching sessions, preferably by a perinatal pathologist with a range of macroscopic and microscopic slides.

3.3.4. Logistics

Although, in other specialties, the declining number of autopsies has minimised exposure to autopsy during training, this does not apply to obstetrics, where perinatal pathology remains predominantly autopsy based. Trainees would be best exposed when attached to a teaching or referral centre with the appropriate perinatal pathology facilities. This should be easy to achieve within Calman rotations.

3.3.5 Subspecialty training in maternal and fetal medicine

There is already considerable exposure to perinatal autopsy in subspecialty training and in most centres there is a period of modular attachment to a perinatal pathologist. Training centres, by definition, will have established working relationships with a perinatal pathologist and regular contact is required through perinatal pathology and perinatal mortality meetings. This high level of exposure in subspecialty training programmes is to be welcomed.

3.3.6 Perinatal pathology meetings

At all levels, attendance at multidisciplinary perinatal pathology or mortality meetings is to be encouraged. These have a major role in encouraging quality and in promoting feedback between obstetricians and pathologists. Obstetricians (and neonatologists) benefit through being familiar with the capabilities and limitations of a perinatal autopsy, and through familiarity with the pathologist's terminology (e.g. syncytial knot formation, chronic villitis of unknown aetiology).

4 PERINATAL AUTOPSY

4.1 Minimum standards

4.1.1 Concept

All perinatal postmortem examinations should be carried out to a protocol. The Royal College of Pathologists' *Guidelines for Postmortem Reports*[27] have set a minimum auditable standard against which quality can be assessed. To date, feedback through the CESDI and regional audits has been associated with an improvement in the quality of reports,[3,6] and it is known that the probability of a postmortem yielding clinically relevant information is directly related to its quality.[4]

4.1.2 Rationale

The rationale is detailed in Section 1.2.2. Standards are needed to ensure that autopsies are performed with an assured minimum degree of thoroughness. In the absence of standards, statements in reports such as 'cardiovascular system normal' yield little useful information. As a general rule, the amount of detail provided reflects the quality of the report.[8] An interpretative summary is important, not just to give an overview but to provide feedback on the indication for the examination.

4.1.3 New standards

The Working Party has reviewed the 1993 minimum standards and revised them as detailed in Appendix I.

4.2 Pregnancy termination

4.2.1 Background

After termination, there is a risk of artefacts leading to limited or potentially erroneous diagnoses.[28] The most obvious is the effect of fixation on soft tissue and limb examination. Other examples of possible erroneous diagnoses of major anomalies include pseudo-encephalocele or anterior abdominal-wall defects, especially with traumatic methods of termination. There are few data to indicate the affect of termination method on the adequacy for pathological examination, although the existing literature suggests that an adequate pathological examination is possible from specimens from most medical methods of termination.

4.2.2 First trimester

Most first-trimester terminations for non-social reasons are of aneuploid fetuses, for which the role of pathology is largely to confirm the karyotype. With increasing uptake of nuchal-translucency scanning, it is likely that a number of karyotypically normal fetuses with major structural anomalies will be identified in the late first trimester, either on echocardiography indicated for nuchal translucency with a normal karyotype[29,30] or on the associated first-trimester anomaly scan.[31] Pathological confirmation after termination for structural anomalies is strongly recommended in order to confirm the diagnosis, to look for additional anomalies that may influence the recurrence risk and for audit. Given that first-trimester anomaly scanning is technically

and diagnostically challenging[32] and has yet to be subject to large-scale audit in a routine setting,[33] it is imperative that first-trimester specimens are examined thoroughly. This is obviously problematic after routine surgical methods, although up to 11 weeks the vacuum catheter can be modified for gentle aspiration under ultrasound control to yield a relatively complete specimen suitable for fetal necropsy.[34] Otherwise, examination of disrupted specimens (even using hand lens or dissecting microscope) will be limited to tissues, limbs and, sometimes, whole organs. It is noteworthy that, in research studies, one group has been able to identify structural heart defects from suction termination samples at 12–15 weeks.[35,36] Medical termination methods, on the other hand, yield the fetus whole. A range of anomalies have been detected using a dissecting microscope in medical termination specimens collected prior to nine weeks of gestation, including neural-tube defects, facial clefts and abdominal-wall defects.[37]

4.2.3 Dilatation and evacuation

In the second trimester, most centres perform medical termination and, provided that the specimen is not fixed, this tends to be regarded as the gold standard. Where dilatation and evacuation are used, the specimen is surgically dismembered and there is understandable concern over the adequacy of examination and, thus, the ability to alter diagnosis or counselling. There are, however, a number of studies showing that pathological examination of such specimens can confirm a wide spectrum of ultrasound diagnoses.[38–40] However, these have the major limitation of yielding less information on additional anomalies. Accordingly, medical methods of termination to allow full pathological examination are recommended for terminations for fetal abnormality, with the exception of aneuploidy and recurrence of previously diagnosed genetic syndromes.

4.2.4 Intracardiac potassium chloride

A number of ancillary procedures have been used during the process of termination of pregnancy. These include installation of substances into the uterus or injection of substances into the fetal circulation. From much older literature, when installation of both prostaglandins and urea was common, there appear to have been no concerns over the adequacy of pathological examination. In line with the recent RCOG recommendation that termination methods after 21 weeks of gestation should ensure that the fetus is born dead,[41] most medical terminations in the last half of pregnancy now involve an intracardiac injection of potassium chloride. There are no data on the effect of potassium chloride on the adequacy of pathological examination. Anecdotal experience is conflicting with some, but not all, centres concerned that potassium chloride accelerates autolysis of cardiac and brain tissue.[42]

4.3 Limited postmortem examination

4.3.1 Rationale

A limited autopsy examination may yield useful information in situations where the parents decline full postmortem. The following investigations may be appropriate:

- external examination
- aspiration of body cavities
- tissue needle biopsy
- targeted open tissue biopsy
- placental pathology
- X-ray
- Ultrasound
- magnetic resonance imaging (MRI).

Incisions can be limited or prior surgical wounds used for access. The extent of the examination will depend on the parents' reasons for declining a full postmortem and their specific consent to each of the components above. There are few situations in which professionals should not recommend a full postmortem but examples include non-mosaic trisomies and third-trimester specimens after first-trimester multifetal pregnancy reduction.

4.3.2 Imaging

An X-ray forms an integral part of every perinatal postmortem, in order to evaluate skeletal maturation, structure and mineralisation, as well as soft tissue calcification and gas accumulation. Contrast administration may facilitate imaging of hollow viscera. Ultrasound has been used to visualise fetal brain, cardiac, lung and renal development where consent to autopsy has been withheld.[43] More recently, MRI has been proposed as an alternative imaging method for this purpose. MRI has the advantage of yielding information different from that obtainable on antenatal ultrasound and, in particular, it gives more detailed information on intracranial structure and neuronal migration. One comparative study showed that pre-autopsy MRI on the dead fetus gave information of comparable sensitivity in 12 of 20 selected cases.[44] Multiplanar reformatting or 'image surgery' of three-dimensional MRI sequences can be used to display soft tissue structures such as the cerebral ventricles or the spinal cord.[45] It is stressed that these techniques remain inferior alternatives to full postmortem with histology by a perinatal pathologist.

4.4 Cytogenetics

4.4.1 Indications

The principal indications are confirmation of antenatally diagnosed chromosomal abnormalities and phenotypic abnormalities suggestive of the possibility of aneuploidy. Many terminations are for chromosomal abnormality and post-termination confirmation of the karyotype is an important quality-control measure. To investigate recurrent (three or more) miscarriages, it is better to karyotype the parents rather than any products of conception. Cytogenetics laboratories may wish to agree a protocol of indications and specimen collection with local obstetricians and paediatric pathologists.

4.4.2 Culture failure

The overall success rate among perinatal tissue specimens in a 1993–94 national audit of cytogenetic laboratories was only 65%, well below the 99% found with other cultured specimens such as chorionic villus samples or

amniotic fluid.[46] Skin specimens were associated with a high culture failure rate (in the region of 60%), double that with other fetal or placental tissues. Fetal skin was particularly difficult to grow after intrauterine death or intrapartum stillbirth. The poor results with skin may have been due to dried, formalin-fixed or partial-thickness samples. Although better success rates were found in termination specimens, even then 25–30% of post-abortal karyotypes in fetal medicine practice fail to grow.[47] Failure appears determined both by tissue type and by the delivery–sampling interval. More recently, national success rates have increased to 72–73%, largely due to improved quality of incoming specimens.[48] Provided that fresh tissue is supplied to cytogenetic laboratories, the method of termination appears not to influence the ability to confirm the diagnosis.

4.4.3 Antenatal karyotyping

Because of the high failure rate with post-abortal karyotyping,[47] antenatal karyotyping is advocated prior to medical termination for fetal abnormality, which (at least prior to 21 weeks) necessitates an additional invasive procedure. Although most aneuploid fetuses have additional abnormalities, these are not always detected antenatally in conditions for which termination might be offered without a karyotype result. Several authors have recommended antenatal karyotyping of apparently isolated fetal neural-tube defects, 13–16% of which are aneuploid.[49,50]

4.4.4 Which tissue?

The principles are as follows. Multiple samples should be collected, in order to minimise the chances of failure. Both fetal and extrafetal tissues (cord/placenta/membrane) should be obtained, because the interpretation of the latter may be complicated by confined placental mosaicism and thus not be indicative of the fetal karyotype. Fresh blood is the ideal specimen for culture but it is not always available. Skin biopsies should be full thickness and placental biopsies should be taken from the central portion, where maceration is least likely.

- Perinatal specimens suitable for karyotyping include:
- placental biopsy from near the site of cord insertion (i.e. to avoid tissue of maternal origin)
- full-depth skin biopsy (including underlying muscle)
- cord or cardiac blood (if possible) in lithium heparin.

If studies of early miscarriage are required, placental villi are cultured if there is no evidence of fetal tissue. However, normal female karyotypes could represent growth of maternal tissue.

4.4.5 Transport

It is important that, whatever the tissue provided, it is as fresh as possible, not macerated and definitely not fixed in formalin. It is also important that tissue does not dry out in transit and most cytogenetics laboratories will provide transport medium. Specimens should be sent to arrive at the laboratory within 24 hours if possible.

4.4.6 Molecular cytogenetics

The techniques of fluorescence *in situ* hybridisation (FISH) or polymerase chain reaction amplification of chromosome specific short tandem repeats may be used on uncultured cells for confirmation of antenatally diagnosed trisomies. Touch preparations are best made from lung (if available) or from placenta.

4.5 DNA Storage

4.5.1 Rationale

The rationale is that malformation syndromes of uncertain aetiology at the time of autopsy may later be shown to have a genetic basis. This could arise when a gene or group of genes is linked to specific malformations or when a subsequent sibling is shown to be similarly affected. Guthrie cards have been used many years later to investigate the cause of postnatal death[51,52] but are only collected on neonatal discharge. In order to investigate the molecular basis of fetal and early neonatal deaths, storage of tissue is required. With rapid advances in determining the molecular basis of disease, including malformation complexes and diseases predisposing to perinatal death (see Section 1.2.4), such material should prove a valuable source for subsequent investigation of the aetiology of perinatal loss, with implications for future reproductive risks in the parents, their offspring and relatives. It is recommended that each perinatal pathology service have a facility for storing fetal tissue and/or DNA.

4.5.2. Logistics

Ideally, DNA should be stored. However, the considerable workload in extracting DNA from a large number of samples, which may never be used, is acknowledged and thus storage of fetal tissue is more practicable. A minute sample is obtained from the fetal liver or the brain (because it has few autolytic enzymes). Specimens are stored in a freezer at minus 80 degrees C, for which consent should be routinely obtained as part of consent to autopsy. Consent for later testing will usually be the responsibility of the clinical geneticist initiating such investigation.

4.5.3 Indications

The ideal would be to store fetal material from all perinatal deaths in which a specific genetic diagnosis had not already been made. The Working Party recommends as a minimum standard that fetal tissue be stored from euploid fetuses with more than one malformation. In addition, it would be good practice to store tissue from selected single anomalies, such as ventriculomegaly, with which a number of genes have already been associated.

4.6 New developments

4.6.1 Genetic disease

A range of phenotypes evident at perinatal autopsy may indicate genotyping for specific conditions. Relevant examples include:

- The microdeletion on 22q11 present in the Di-George or velocardiofacial syndromes should be sought by FISH in cases of cardiac conotruncal anomalies.[53]

- Large expansion of the normal myotonic dystrophy CTG triplet repeat is responsible for the congenital and often lethal form of myotonic dystrophy, characterised by polyhydramnios, pulmonary hypoplasia, talipes and joint contractures. This is inherited from the mother, who may only be mildly affected and thus asymptomatic.[54]
- Thanatophoric dwarfism is due to a variety of mutations in the fibroblast growth factor receptor-3 gene.[55]
- Cystic fibrosis mutation testing in cases associated with meconium peritonitis.
- FISH testing for the submicroscopic deletion of 17p13 responsible for most cases of the Miller–Dieker syndrome of defective neuronal migration is indicated where lissencephaly (literally smooth brain) is suspected.[56]
- Spinal muscular atrophy, the second most common lethal autonomic disorder after cystic fibrosis, is due to deletions in the SMN gene. The type 1 form can cause pulmonary hypoplasia and perinatal death.
- Medium Chain Acyl-CoA dehydrogenase deficiency may cause a metabolic-type death in the perinatal period and is commonly due to the G-985 mutation in theMCAD gene.

4.6.2 Thrombophilias

Although the acquired thrombophilias associated with the lupus inhibitor and anticardiolipin antibodies have been well recognised as causing fetal loss, only recently have similar associations been made with hereditary thrombophilias. Factor V Leiden, hyperhomocysteinaemia due to homozygosity for the thermolabile methyltetrahydrofolate reductase variant and protein S, C and antithrombin deficiencies are known for their association with maternal venous thrombosis. However, studies increasingly implicate the hereditary thrombophilias in over 50% of adverse obstetric outcomes such as abruption, severe pre-eclampsia and fetal death.[57,58] The mechanism is likely to be thrombosis and infarction at the placental site. The risk appears particularly great with multiple maternal defects or with fetal homozygosity.[58,59] The exact role of genotyping following perinatal death or complications associated with placental thrombosis remains to be determined, as is the appropriate preventative therapy in any future pregnancy.

4.6.3 Infection

Molecular testing may have a role in establishing the presence of non-bacterial infection in perinatal tissue samples analysed many weeks after primary fetal infection. Although immunocytochemistry remains the main method of diagnosing transplacental infection, demonstrating the presence of viral and protozoal DNA or RNA may have a complementary or confirmatory role, especially in macerated samples. Examples include toxoplasmosis, parvovirus, varicella and cytomegalovirus. Recent data have implicated these and other viruses, such as adenovirus and enterovirus, in a range of fetal pathologies, including growth restriction, unexplained stillbirth and hydrops.[60,61]

4.6.4 Unexplained stillbirth

With the decline in perinatal deaths from other causes, unexplained antepartum stillbirth is now more common than deaths from prematurity or

sudden infant death syndrome.[62] As in the case of sudden infant death syndrome, the value of a rigorous postmortem is in excluding possible causes, such as fetomaternal haemorrhage, and suboptimal fetal growth in babies with birthweights above the fifth centile.[63] Postmortem led to the clinical diagnosis being revised in 12% of cases of otherwise apparently unexplained stillbirths over 1 kg in the 1999 CESDI audit.[6]

4.7 Quality assurance

4.7.1 Perinatal mortality meetings

Clinicopathological conferences are important forums in which obstetricians and paediatricians can influence the quality of postmortem reports by providing appropriate and adequate clinical information and by subjecting the pathological findings and the pathologist to the same scrutiny as is the obstetrician regarding clinical management. Unfortunately, these meetings often focus on obstetric management as understood by the obstetric audience, with the views of the pathologist accepted uncritically.

4.7.2 Audit

The Working Party supports the Service Specification for Specialist Perinatal Pathology Services, requiring that they issue an annual report to purchasers on workload and audit figures.[21]

5 PLACENTAL PATHOLOGY

5.1 Indications

5.1.1 Current practice

For live births, the 1988 Joint College Report on Fetal and Perinatal Pathology[1] recommended that placentas from the following pregnancies should be examined by a pathologist: very-low-birthweight (less than 1500 g), small-for-gestational-age (less than the third centile for age and sex), multiple pregnancy and 'any abnormal pregnancy'. There is little information available on the extent to which these guidelines are being followed. In one region, there was no mention of placental examination in 11% of pathology reports after stillbirth and 76% after early neonatal death.[8]

5.1.2 Role

Macroscopic and histological examination of the placenta has an important role in delineating the cause of obstetric and neonatal pathologies. In addition to clinical relevance, it has implications for risk management and audit. Chorioamnionitis is well recognised as a cause of preterm labour but it is increasingly implicated in inflammatory cytokine-mediated periventricular leucomalacia.[64–66] Placental infarcts and retroplacental haemorrhage give insights into fetal condition, especially in maternal diseases such as pre-eclampsia, diabetes and the thrombophilias. The adequacy of trophoblast invasion can be inferred from study of the basal plate. Hypocoiled or straight umbilical cords have been associated with fetal distress and intrauterine death.[67,68] Rare findings include chorioangiomas, metastases, fetus papyraceous, aberrant cord insertions and non-bacterial villitis. Placental examination is indicated in multiple pregnancy, both because of the high incidence of intrauterine growth restriction, preterm labour and neurological sequelae and because of complications specific to twin and higher-order multiple pregnancy.

5.1.3 Indications

The Working Party reaffirms the previous indications for placental examination by a pathologist but, in addition, extends them to pregnancies with:

(i) neonatal hypoxic ischaemic encephalopathy
(ii) early neonatal sepsis
(iii) preterm labour at less than 34 weeks
(iv) congenital malformations
(v) macroscopic placental abnormalities
(vi) recurrent antepartum haemorrhage
(vii) clinical chorioamnionitis
(viii) established maternal diabetes
(ix) severe pre-eclampsia.

It is appreciated that indications (i) and (ii) above, as well as small-for-gestational-age, will not always be obvious at the time of delivery. This means that a system of storing placentas for the first few days will be needed.

5.2 Multiple pregnancy

5.2.1 Chorionicity and zygosity

Chorionicity should be confirmed in all, both macroscopically and histologically. Establishing chorionicity is of relevance to antenatally acquired brain injury and to confirming or excluding twin to twin transfusion as a cause of the stuck-twin syndrome. It also has a role in auditing antenatal determination of chorionicity by ultrasound, an important management strategy in reducing the perinatal complications of monochorionic twins. In like-sex twins, chorionicity also informs zygosity, although around 20% of like-sex dichorionic twins will still require DNA testing. This no longer requires cord blood collection. Instead, specimens of buccal mucosa can be obtained later if and when the parents want zygosity testing.

5.2.2 Vascular anastomoses

Monochorionic twins have 3–10 times the fetal and perinatal loss and neurological morbidity rate of dichorionic twins and carry greater perinatal risks than triplet pregnancies.[69] These risks are largely attributed to almost ubiquitous placental vascular anastomoses between the twins' circulations.[70] Injection studies have, to date, largely been confined to research settings but are increasingly becoming best practice, as they explain the transfusional complications of monochorionic twins. Superficial anastomoses are implicated in the sequelae of single intrauterine death,[71] and absent artery-to-artery anastomoses in twin to twin transfusion syndrome.[70]

6 CONSENT

6.1 Pathological examination

The Working Party supports the recent advice issued by CESDI to professionals on the fetal and infant postmortem[10] and the RCPath's recent Guidelines for the Retention of Tissues and Organs at Post-Mortem Examination.[11]

6.1.1 Autopsy

Low autopsy rates have been attributed to:

(i) difficulty in discussing this with parents during the acute distress which follows bereavement
(ii) consent being sought by uninformed professionals
(iii) the personal and religious objections of some parents to necropsy.

On the one hand, parental refusal must remain a right but on the other, parents also have rights to both (a) a high quality autopsy and (b) an informed professional offering them the autopsy.[72] Providing (a) and (b) are achieved, the Working Party feels it inappropriate to recommend a target autopsy rate. A 75% rate, for instance, would be unlikely to be achieved in areas of the country with large Muslim populations. Instead, it would be more appropriate to audit the quality of the offer as well as the autopsy itself.

6.1.2 The process

Obtaining consent to autopsy is usually the duty of the obstetrician (or neonatologist), not the pathologist. It should be the responsibility of a senior member of the clinical team, not the most junior. The person obtaining consent should be familiar with the role and conduct of perinatal autopsy, as well as its application in an individual case. Discussion with the perinatal pathologist may be helpful in particular cases, prior to approaching the parents. Parents should be aware that the autopsy may:

- confirm clinical diagnoses
- reveal the cause(s) of death
- identify structural anomalies of relevance to the risk of recurrence
- provide an estimate of the time of death
- identify chronic intrauterine disease (infection, brain damage, etc.)
- give information on the complications of treatment.

In particular, parents need to be aware that it may be difficult, if not impossible, to advise on the risk of recurrence in a future pregnancy in the absence of an autopsy. Consent is necessary for:

(i) the postmortem examination and tissue retention for small samples for diagnostic histology
(ii) the use of material for teaching, research and tissue retention for treatment of others
(iii) organ retention.

The Royal College of Pathologists has recently recommended that hospitals provide an information leaflet for relatives explaining the purpose of an autopsy, the medical benefits of tissue and organ retention and their rights to grant or withhold their agreement. The CESDI document *Guide to the Post*

Mortem Examination: Brief Notes for Parents and Families Who Have Lost a Baby in Pregnancy and Infancy[73] is recommended in this regard.

6.1.3 Fetal pathology

Consent for postmortem is required for all live births, regardless of gestation, whereas after intrauterine death or fetal loss it is only legally necessary for stillbirths, defined as being 24 or more weeks of gestation. However, perception of fetal loss has changed in recent years. In many centres, consent has been obtained for all fetal examinations, with little additional difficulty encountered in requesting postmortem – even for very small fetuses. This practice should now be universal, as recently recommended by the Royal College of Pathology.[11]

6.1.4 Limited autopsy

Parents reluctant to give consent to full postmortem may be offered a limited postmortem. This can be of value if directed to answering specific questions, e.g. the details of a structural abnormality. The number and range of investigations detailed in Section 4.3.1 will depend on the clinical situation and parental consent. Parents should specifically consent to any invasive procedure or biopsy on the fetus. Consent for tests on the placenta is not routinely sought, as this is considered a surgical specimen. Where parents decline full postmortem, however, obtaining consent for placental examination is good practice.

6.1.5 Organ/tissue retention

Perinatal autopsy invariably requires the collection of a wide range of tissue samples for histology. However, in some circumstances, it is good practice to retain a whole organ for later detailed examination. The heart and brain are the most likely organs to be retained. Congenital heart disease, which may have been subject to surgery, can be very complex and for complete understanding may need study by specialists other than the pathologist conducting the postmortem. A similar need for specialist input is often required for the brain. Where an intracranial abnormality has been identified, e.g. by ultrasound, attempted examination at the time of the autopsy may fail and thus no diagnosis be obtained. It is now essential practice to obtain specific consent for whole-organ retention.11 While this may seem a difficult question to pose to parents, experience has shown that parents will often consent if they are provided with a full explanation as to its necessity. Conversely, extreme distress can be caused by later discovery that organs have been retained without parental knowledge. In the past, it has not been usual to specify explicitly that whole organs might need to be retained. This is no longer acceptable, as stated in the Royal College of Pathology guidelines.11 When agreement is obtained for organ retention, its ultimate fate should be discussed. Where feasible, organs are reunited with the body, prior to burial or cremation. When this is not possible, parents can choose either to make their own arrangements or for the hospital to dispose of the organs after investigations have been completed. It is now essential that detailed records are kept of any tissue samples that are retained or discarded. Although these recommendations comply with recommended standards in 2001, it will be important for both obstetricians and pathologists to remain

abreast of new guidelines and legislation as they are produced by the Chief Medical Officer and others.[74]

6.1.6 Transport

Bodies often need to be transported from the place of delivery or death to a regional centre for specialist autopsy by a perinatal pathologist. Parents should always be informed of this transfer, for which consent should be sought. The parents should be aware of the means of transport and when the body will be returned. The Royal College of Pathologists' Service Specification for Perinatal Pathology Services requires that providers have written procedures for the handling, receipt and return of bodies.[21]

6.1.7 Coroner's autopsy

The coroner has a legal responsibility to investigate death in a number of circumstances, usually where death is unexpected and the doctor cannot sign a death certificate. In perinatal and paediatric pathology, this applies mainly to sudden infant deaths at home and deaths within 24 hours of surgery, but also to violent deaths such as after road traffic or other accidents involving the baby or mother when pregnant. Informing the coroner does not automatically mean that an autopsy will take place and discussion of the individual case may lead the coroner to authorise the issue of a death certificate. As part of the investigation, the coroner will probably request an autopsy, which may be performed by a local pathologist, although, increasingly, a specialist paediatric or forensic pathologist is commissioned. Parental consent is not required for coroner's autopsies. However, parents have the right to expect the same standard of explanation as for a non-mandated perinatal autopsy. The coroner should be informed if there is a legal requirement to do so but this process should not be used to circumvent parental refusal for autopsy. Whenever possible, discussion with the coroner should take place before discussion with the parents. Parents should be kept informed of any tissues or organs retained and given the chance of having them returned once released by the coroner.

6.2 Use of fetal tissue in research and therapy

6.2.1 Polkinghorne guidelines

Research on fetal tissues and the use of fetal tissue for innovative therapies may only be carried out if it conforms to the 1988 Polkinghorne guidelines.[75] These were reaffirmed in further Department of Health advice in 1995.[76] Local ethics committees are required to scrutinise protocols involving fetal tissue for compliance with the guidelines. Its fundamental ethical principle is that the decision to terminate a pregnancy and the method and timing of the abortion must not be influenced by consideration of the possible use that may be made of the tissue.

6.2.2 Consent

The mother's written consent is required but should only be sought after she has given consent to the termination. There should be no inducement put to the mother that may influence her decision and she 'should not be informed of the specific use which may be made of the fetal tissue or whether it is to be

used at all'. The report also stated that 'it may be desirable to consult the father as some tests on fetal tissue may reveal a finding of potential significance to him and because he may have knowledge of a transmissible or hereditary disease but his consent is not a requirement nor should have the power to forbid research or therapy making use of fetal tissue'.

6.2.3 Separation of source from supply

The guidelines recommended that the supply of fetal tissue be separated from the practice of research and therapy. In response, the Medical Research Council (MRC) Fetal Tissue Bank was established at Hammersmith Hospital, London, as a national resource from which researchers could obtain tissue separated from the source of supply. Department of Health guidelines acknowledged situations in which use of the MRC Tissue Bank would be inappropriate, such as where fresh tissue was needed. The gave guidance on the appropriate local arrangements where tissue need to be obtained locally and, in particular, that local ethics committees ensure compliance with the Polkinghorne principles. Specifically, those involved with the process of abortion should not knowingly be involved in the research on the fetus or fetal tissue collected.

6.2.4 Logistic difficulties

The Polkinghorne recommendations now seem outdated, being made in the 1980s when standards of consent were less rigorous and before the development of modern fetal medicine techniques. Firstly, preventing consent being informed as to the use of the tissue is out of keeping with modern standards of consent and modern consumer expectations. Secondly, the rigorous restrictions to separate source from supply impede fetal research and thus advances in care, in a way not envisaged by the Polkinghorne Committee. This applies to research undertaken at termination using novel collection techniques (for example, embryoscopy, coelocecentesis, yolk-sac aspiration, fetal blood sampling). Access to the first-trimester circulation, in particular, allows study of early fetal and placental development and provides a ready source of pluripotent stem and progenitor cells of relevance to non-invasive prenatal diagnosis, fetal stem-cell transplantation and gene therapy.[76] Such research necessarily involves fetal medicine specialists. Their preclusion from involvement in the termination process creates formidable logistic barriers to research in this area. The Working Party accepts that clinicians involved in the decision-making process regarding termination should not normally be involved in the resultant fetal tissue research. However, it recommends that the guidelines for research on fetal tissues be updated to take account of fetal tissue collection via specialised procedures at the time of termination of pregnancy.

7 INFORMATION TECHNOLOGY

As in other branches of medicine, advances in information technology provision are likely to have significant impact on the provision of perinatal pathology services. On the one hand, there will clearly be increasing use made of desktop computers, graphics, the internet, information databases and electronic storage systems. On the other hand, the extent to which video-conferencing systems and the NHS-Wide Network are used is likely to depend on more general funding and infrastructure issues within the NHS (the NHS-Wide Network is a secure private network based on internet technologies, through which all hospitals and general practitioners will be connected by 2002[78]).

7.1.Necropsy reports

7.1.1 Standardisation

One way to ensure compliance with minimum data sets such as recommended by the Royal College of Pathologists and updated here is to make a standard pro forma for perinatal autopsy requests and reports available for downloading from the worldwide web; for example via PDF (portable document format) using Acrobat® Reader. Electronic pro formas are flexible and may be modified for different types of examination (such as mid-trimester miscarriage, term neonatal death).

7.1.2 Pictures

Photographs can be made available as an integral part of the report, either directly from digital cameras or, as an interim measure, scanned from conventional still pictures. In selected cases, digital video clips may add additional information (cardiac anomalies, injection of placental anastomoses). These would increase the relevance of reports to clinicians, an important step in tackling low autopsy rates. A disadvantage could be parental abreactions if disclosed. To prevent this, an edited copy could be made available, although, in line with the principles of freedom of information and the Data Protection Act, many patients expect, and are entitled to, full disclosure.

7.1.3 Transmission

Electronic transmission by email, the internet and the NHS-Wide Network will minimise delay and administrative error. Providers may wish to make reports available on line via the worldwide web, subject to suitable security protection to maintain confidentiality.

7.2 Telemedicine

Still images of pathology slides or macroscopic specimens can be transmitted for specialist opinion via email, the internet or NHS or institutional intranets, such as the Joint Academic network (JANET). Telemedicine involving consultation in real time has been applied to several areas of health care. However, uptake has been slow, largely due to the start-up costs of hardware and the line costs with wideband ISDN lines.[79] The cost of desktop

PC-based video-conferencing equipment capable of running on ISDN2 or ISDN6 lines is likely to fall and their uptake for trusts is likely to be a general policy issue across many branches of medicine. An obvious application of telemedicine in this area is use by general pathologists to consult over a particular specimen with a distant subspecialist fetal and perinatal pathologist. As experienced in fetal telemedicine, this may be an important initiative in reducing the incidence of false negative diagnoses.[80]

7.3 Information access

Pathologists will increasingly gain access to information on line, as currently available free on the worldwide web to Medline via PubMed (www.ncbi.nlm.nih.gov/PubMed/) and to Online Mendelian Inheritance in Man (www.ncbi.nlm.nih.gov/Omim/). Many NHS regions now provide free access to their staff to the Cochrane Collaboration. Policy documents from professional bodies such as Royal Colleges are increasingly available through College websites. Other relevant information systems are available either commercially or via institutional affiliations (for instance, the London Dysmorphology and Neurogenetics Databases). Others, such as Platypus, POSSUM, the Radiological Electronic Atlas of Malformation Syndromes (REAMS) and the Human Cytogenetics Database are currently only available on CD-ROM.

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APPENDIX 1

Minimum standards for postmortem examination after fetal and perinatal death

External examination

- Bodyweight (to nearest gram if less than 5 kg)
- Head circumference
- Crown–heel and crown–rump lengths
- Foot length
- Apparent gestation
- Maceration (if baby born dead)
- Dysmorphic features/congenital malformations and deformities
- Other abnormalities (oedema, abnormal pallor, meconium staining, etc.)

Internal examination

- Comment on cranial, thoracic and abdominal cavities
- Systematic description of major organs and tissues
- Weights of all major organs on digital balance (to 0.1 g)
- Comment on skeleton
- Measurement of abdominal and thoracic fat thickness

Placenta

- Size
- Trimmed weight
- Umbilical cord (length, vessels, abnormalities)
- Membranes (complete, incomplete, abnormalities)
- Fetal, maternal and cut surfaces

Histology

- At least one block of all major thoracic and abdominal organs (right and left lungs, liver, kidney, thymus, adrenals and pancreas)
- Costochondral junction (over 24 weeks of gestation)
- Adequate sampling of brain (varies with case; minimum of one block from hind brain and one from cerebral hemispheres)
- Adequate sampling of placenta (cord, membranes, focal lesions, grossly normal parenchyma to include amnion and decidua)

Special procedures and investigations

- X-ray mandatory for suspected skeletal dysplasia and multiple malformations without antemortem diagnosis
- Photography mandatory for dysmorphic fetuses and babies without antemortem diagnosis; advised for other gross abnormalities
- Bacteriology (blood/spleen/lung/cerebrospinal fluid), if clinically indicated
- Virology, if clinically indicated
- Karyotype, if clinically indicated
- Storage of fibroblasts/frozen tissue/DNA, if clinically indicated
- Biochemistry, if clinically indicated
- Haematology, if clinically indicated

Postmortem report

- Demographic details
- Clinical history
- Systematic description of external, internal and placental examination, and results of X-ray and other ancillary investigations
- Record of photographs and any samples retained
- Summary of major findings including sex and apparent gestation, estimated timing of death in babies born dead, adequacy of growth and nutrition, presence/absence of cogenital malformation, major pathological lesions, evidence of chronic stress or disease prior to death, placental examination
- Commentary addressing clinical questions and significance of pathological findings
- Mode/cause of death
- A provisional report on the macroscopic findings should be issued within 24–48 hours of the autopsy, with the histology and further investigations incorporated into a final report when available
- Timely dispatch to clinicians

The above document is available on both Colleges' websites.