The Royal College of Pathologists

Pathology: the science behind the cure

Guidelines on Autopsy Practice

Scenario 10: Neonatal death

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In accordance with the College pre-publications policy, this document was put on The Royal College of Pathologists' website for consultation from 14 October to 4 November 2005. Three pieces of feedback were received. Dr Chris Wright and Professor Sebastian Lucas considered the feedback on behalf of the Working Party of the Autopsy, and amended the document accordingly. Please email publications@rcpath.org if you wish to see their responses to the feedback received.

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Director of Publications

Many of the aetiological and pathogenetic factors that are important in stillbirth are clearly also relevant to neonatal death, and there is therefore considerable overlap in the approach to these two situations (see 'Scenario 9: Stillborn infant').

The role of the autopsy

- To establish factors (both in utero and post partum) contributing to death and (if possible) the immediate cause of death.
- To identify concomitant diseases, particularly those with implications for subsequent pregnancies (e.g. growth restriction, malformation, maternal diabetes).
- To confirm or exclude iatrogenic disease, including both birth trauma and complications of neonatal management.
- To provide information for audit purposes (e.g. cranial ultrasound).

Pathology encountered at autopsy

- Effects of hypoxia (occurring ante, intra or post partum), in particular hypoxic-ischaemic encephalopathy.
- Growth restriction: symmetric, asymmetric (nutritional).
- Infection (predominantly septicaemia, pneumonia, meningitis): acquired in utero or post partum, including infections complicating invasive neonatal management.
- Malformation.
- Complications of prematurity, including:
  - hyaline membrane disease and its sequelae
  - CNS disease (germinal matrix haemorrhage, white matter infarction)
  - necrotising enterocolitis, etc.
- Iatrogenic disease:
  - birth trauma: cranial, extracranial
  - due to neonatal management: intubation/ventilation, chest drains, vascular access, medication, etc.
- Blood loss (in utero/neonatal, external/internal).
- Hydrops.
- Effects of maternal disease, e.g. diabetes, hypertension/pre-eclampsia.
- Metabolic disease, e.g. urea cycle defect, fatty acid oxidation defect.
- Placental and cord disease (see 'Scenario 9: Stillborn infant').

Specific health and safety aspects

The pathologist needs to know the results of the antenatal infection screens.

In regions of high maternal HIV prevalence, autopsy practice using universal precautions will significantly protect against accidental transmission.

Clinical information relevant to the autopsy

Wherever possible, the neonatal and (where relevant) obstetric hospital notes should be made available.

Information required is as for 'Scenario 9: Stillborn infant', plus:

- condition at birth (cord pH, Apgar scores, etc.)
- clinical course following delivery, including methods of resuscitation and intensive care (including use of chest drains and vascular cannulae).

The autopsy procedure

- Requires availability of appropriately sized instruments; balances for weighing body (i.e. up to approximately 6 kg) and organs (to nearest 0.1 g); charts of normal values (baby and placenta).
- Whole body X-ray (for gestational assessment, malformation, pathological gas collections, position of cannulae and drains, etc. Mandatory for suspected skeletal dysplasia).
- Photography to document external and internal abnormalities,
- Routine external body measurements (body weight, crown-rump length, crown-heel length, foot length, occipitofrontal circumference),
- Detailed external examination, including: nutritional status/soft tissue and muscle bulk; presence of oedema (localised/generalised), pallor, meconium staining, jaundice or dysmorphism; evidence of trauma, siting of chest drains and vascular cannulae and other iatrogenic lesions. Report should include a description of external morphology mentioning specifically: fontanelles, eyes, ears, nose, patency of choanae, palatal fusion, spine, limbs, digits, palmar creases, external genitalia, patency of anus, umbilical cord.
- T- or Y-shaped incision; measurement of sternal fat thickness.
- CNS examination:
  - paramedian skull incisions to allow assessment of falx and venous sinuses
  - assessment of falcine and tentorial injury and meningeal haemorrhage prior to brain removal (suspected intrapartum trauma)
  - exclusion of skull fracture by direct inspection; and spinal injury by posterior approach (suspected intrapartum trauma)
  - if suspected CNS malformation (including ventriculomegaly): examination of posterior fossa structures by posterior approach
  - observation of gyral pattern to assist gestational assessment.
- Detailed systematic examination of other internal organs, including:
  - identification of pneumothorax (chest incision under water)
  - positioning of chest drains
  - umbilical arteries and vein, ductus venosus (exclude trauma/thrombosis secondary to cannulation)
  - in situ examination of the heart and great vessels with sequential segmental analysis of malformations
  - thoracic and abdominal organs removed in continuity or in blocks (if the latter, care is needed to assess structures (normal and abnormal) crossing diaphragm)
  - weights of all major organs including thymus.
- Detailed examination of placenta and umbilical cord (as per 'Scenario 9: Stillborn infant'): can be helpful in assessing aetiology and time of onset of infection or hypoxic-ischaemic encephalopathy; this may be of benefit in resolving issues of medicolegal interest. Placentas should be sent for examination when a baby is born preterm and/or in poor condition, or when there is evidence of infection, growth restriction, malformation or other significant abnormalities. Some units have mechanisms in place to allow storage of placentae for at least several days so that they can be retrieved if infants become unwell in the neonatal period.

Note: Ward staff should be asked to leave cannulae, drains, etc. in situ as far as possible, to allow assessment of their internal disposition. They can be cut flush with the skin if necessary.

Specific significant organ systems

None.

Organ retention (with appropriate informed consent)

- Organs with congenital malformations (particularly heart) if input not available from perinatal pathologist and abnormality cannot be satisfactorily recorded by photography.
- Brain for macroscopic and histological assessment of hypoxic-ischaemic injury (timing, extent and severity), haemorrhage, malformation, infection, etc. Depending on circumstances, brain retention and possibly referral for specialist neuropathology may be indicated. However, submersion for several days, either in formalin with 5% acetic acid at room temperature or in 40% formalin at 37ºC, may produce sufficient fixation to allow adequate sectioning and block sampling if the brain is to be returned to the body before release.
- The consent form must be carefully checked for consistency with respect to tissue retention and achieving the aims of the autopsy. Permanent archiving of tissues blocks and slides should be the norm.

Minimum blocks for histological examination

- Thymus.
- Heart (including papillary muscle).
- Trachea/thyroid.
- Lungs (at least two from each lung).
- Small and large intestine.
- Liver.
- Pancreas.
- Adrenal gland.
- Kidney (x 2).
- Costo-chondral junction (assessment of growth plate and bone marrow); bone histology mandatory for suspected skeletal dysplasia.
- Brain: when systematically assessing hypoxic-ischaemic injury blocks should if possible include: cerebral cortex and periventricular white matter, deep grey matter, hippocampus, midbrain (inferior colliculi), pons, medulla (inferior olives), cerebellum with dentate nucleus. Sampling may by necessity be more restricted if there is advanced autolysis. In cases of malformation, appropriate extensive sampling should be done.
- Other organ lesions as indicated by history or macroscopic findings.
- Placenta (at least two full-thickness blocks, plus focal lesions).
- Membrane roll.
- Cord (at least two).

Other samples required

- Bacteriology: lung, blood, cerebro-spinal fluid, other (as dictated by clinical history or macroscopic findings).
- Samples for genetics, virology, biochemistry, haematology if indicated by history or macroscopic findings. In particular, with sudden unexpected neonatal death the possibility of metabolic disease should be considered and appropriate minimum samples would include: blood, blood spots (Guthrie card), skin (for fibroblast culture, i.e. not frozen), urine, and tissue for freezing (liver, muscle, etc. as indicated).
- For details on investigation of metabolic disorders, consult the Neonatal Metabolic Biochemistry Network website.[4]
- These samples should be taken as soon as possible after death to reduce deterioration.

The clinico-pathological summary

Should include:

- an assessment of organ development relative to gestation and age at death
- a summary of the major findings
- a discussion of the aetiology/pathogenesis of these findings, and the timing/sequence of events leading to death (recognising that neonatal deaths are frequently multifactorial and may not be attributable to a single cause of death)
- explicit statements regarding the presence/absence of malformation and infection and (where appropriate) growth restriction and trauma (negative findings are helpful and may be crucial)
- identification of those cases with an increased risk of recurrence (including malformation syndromes, growth restriction and maternal diabetes).

Specimen cause of death opinions/statements

- Spontaneous vaginal delivery at term; early neonatal death at age 12 hours due to total anomalous pulmonary venous connection.
- Maternal pre-eclampsia; intrauterine growth restriction; delivery by emergency section at 29 weeks gestation for deteriorating fetal condition; hyaline membrane disease and large germinal matrix haemorrhage; late neonatal death at age 14 days due to pseudomonas pneumonia and septicaemia.
- Spontaneous labour at 38 weeks gestation; attempted ventouse delivery for prolonged second stage; shoulder dystocia; fetal macrosomia with islet hyperplasia; early neonatal death at age 10 hours due to hypoxic-ischaemic encephalopathy and cranial trauma.

References

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2. Keeling JW. The perinatal necropsy. In: Keeling J (editor). *Fetal and Neonatal Pathology*. London: Springer, 2001. pp. 1–46.
3. Bove KE. Practice guidelines for autopsy pathology – the perinatal and pediatric autopsy. *Arch Pathol Lab Med* 1997;121:368–376.
4. Neonatal Metabolic Biochemistry Network website. www.metbio.net

The RCPath Working Party on the Autopsy

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